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The American Heart Journal

CONTENTS FOR APRIL, 1936

Original Communications

Pulse Wave Velocity and Arterial Elasticity in Arterial Hypertension, Arteriosclerosis, and Related Conditions. Florence W. Haynes, Ph.D., Laurence B. Ellis, M.D., and Soma Weiss, M.D., Boston, Mass. ---- 385

The Relation of Arterial Pulse Pressure to the Hemodynamics of Arterial Hypertension. Soma Weiss, M.D., Florence W. Haynes, Ph.D., and Rose Shore, A.B., Boston, Mass. ---- 402

Some Cases of Slow Pulse Associated With Electrocardiographic Changes in Cardiac Patients After Maximal Work on the Krogh Ergometer. E. Bierring, Kaj Larsen, and E. Nielsen, Copenhagen, Denmark ---- 416

Acrocyanosis: A Study of the Circulatory Fault. Albert H. Elliot, M.D., Richard D. Evans, M.D., and Caleb S. Stone, M.D., Santa Barbara, Calif. 431

Double Aortic Arch With Total Persistence of the Right and Isthmus Stenosis of the Left Arch: A New Clinical and X-Ray Picture. Aaron Arkin, Ph.D., M.D., Chicago, Ill. ---- 444

The Velocity of the Blood Flow in Therapeutic Hyperpyrexia. Israel Kopp, M.D., Boston, Mass. ---- 473

Department of Clinical Reports

An Unusual T-Wave in an Electrocardiogram. Robert H. Halsey, M.D., New York, N. Y. ---- 489

Electrocardiographic Changes in Trichinosis. E. H. Cushing, M.D., Cleveland, Ohio ---- 494

Department of Reviews and Abstracts

Selected Abstracts ---- 497

Book Reviews ---- 511

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The American Heart Journal

VOL. 11 APRIL, 1936 NO. 4

Original Communications

PULSE WAVE VELOCITY AND ARTERIAL ELASTICITY IN ARTERIAL HYPERTENSION, ARTERIOSCLEROSIS, AND RELATED CONDITIONS*†

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BOSTON, MASS.

THE elasticity of the arteries exerts a significant influence on the peripheral vascular resistance and on the blood flow. Other factors such as arteriolar resistance, cardiac output, circulating blood volume, and blood viscosity being constant, the more elastic the arteries the lower will be the systolic and pulse pressures, the less the work of the heart, and the more uniform the blood flow to the capillaries.

In man the arterial elasticity may be estimated in vivo from the pulse wave velocity since the less extensible the artery the greater is the pulse wave velocity. Bramwell and Hill[1] have shown that, barring variations in the blood flow, the extensibility of an artery may be expressed as follows:

$$\text{Percentage increase in volume per mm. Hg increase of pressure} = \frac{12.7}{(\text{velocity in meters per second})^2}$$

The chief factors which alter the arterial elasticity, namely, (1) the condition and constitution of the arterial wall and (2) the effective pressure within the artery, have been recently discussed in some detail by Hallock[2] for normal subjects. The changes found by various observers in the pulse wave velocity in pathological conditions have been summarized in Table I.

We have made pulse wave velocity and oscillometric measurements in different parts of the body in an attempt to evaluate the arterial elasticity in hypertension and arteriosclerosis, in which conditions a priori the elastic properties of the vessels may be expected to be significantly

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†This investigation was aided in part by a grant from the Josiah Macy, Jr., Foundation.

TABLE I

OBSERVATIONS IN THE LITERATURE OF THE CHANGES IN THE PULSE WAVE VELOCITY IN HYPERTENSION, ARTERIOSCLEROSIS, AND OTHER PATHOLOGICAL CONDITIONS

AUTHOR	DATE	METHOD OF RECORDING PULSE WAVES	VELOCITY MEASURED	NORMAL VALUES (METERS PER SEC.)	HYPERTENSION	ARTERIOSCLEROSIS	OTHER CONDITIONS
Friberger[3]	1912	Optical	Subclavian-radial.	Young controls 6.7-10.4 Average 8.2 (22 persons)	Increased in cases with highest blood pressure (nephritis). 8.6-14.5 Average 11.8 (9 cases)	Possibly slightly increased over controls of the same age. 7.0-10.1 Average 8.8 (14 young cases) Not proportional to the amount of palpable thickening but possibly greater in cases with poor pulsation.	
Ruschke[4]	1912	Optical	Carotid-radial.	9		Increased 9-12 Average 10.4 (8 cases)	*Aortic and mitral insufficiency*—often slightly decreased and lower if decompensated (14 cases). *Nephritis*—10-14 (5 cases). *Scattered cases* of anemia, chlorosis, tuberculosis, carcinoma, neurasthenia and hypotension; all rather low.
Münzer[5]	1912	Kymograph	Upper arm to calf. Figures given for heart to calf.	9-12	Greatly increased. 14.5-23 (4 cases)	Increased in 1 of 3 cases reported. 7.2-16.5	*Scattered cases* of mitral insufficiency, hemophilia, polycythemia—normal. Hypotension and aortic insufficiency —low.

TABLE I—CONT'D

Silberman[6]	1913	Kymograph	Upper arm to calf.	5.1 (1 person)		Variable on different days. 4.6-8.1 (2 cases)	*Scattered cases* of aortic insufficiency, septicemia, hyperthyroidism, gout, and gastric ulcer—very variable.
Laubry, Mougeot, and Giroux[7]	1921	Kymograph Curves low	Subclavian-radial I. Femoral-tibial II. In some cases subclavian-femoral.	Young controls I. 7.9-9 II. 9-10	Compensated (5 cases). I. 11.6 II. 16.4 Insufficiency of left ventricle (10 cases). I. 10.0 II. 14.5 Blood pressures very high. When velocity does not follow systolic pressure it means insufficiency of left ventricle.	Three cases with hypertension reported. Aorta may be rigid and peripheral arteries relatively unaffected.	*Hypotension*—decreased velocity. *Pulsus alternans*—speed of feeble beat less than that of strong one. *Extrasystole*—decreased velocity in premature beats.
Bramwell and Hill[8]	1922	Hot wire sphygmograph	Carotid-radial.			Theoretically increased.	*Scattered cases* of aortic incompetence, heart-block, etc., of different ages. *Aneurysm*—velocity decreased.
Sands[9]	1924	Optical	Apex-brachial I. Brachial-radial II. Apex-radial III. Apex-femoral IV. Femoral-dorsalis pedis V. Apex-dorsalis pedis VI.	I. 3.84 II. 7.66 III. 4.90 IV. 3.93 V. 8.44 VI. 5.61 (51 persons)		Two groups of patients: 1. Velocity increased in aorta but decreased in peripheral vessels. 2. Velocity increased in both central and peripheral vessels.	*Aortic regurgitation*—no change and no correlation with diastolic pressure. *Hyperthyroidism*—no change.

TABLE I—CONT'D

AUTHOR	DATE	METHOD OF RECORDING PULSE WAVES	VELOCITY MEASURED	NORMAL VALUES (METERS PER SEC.)	HYPERTENSION	ARTERIOSCLEROSIS	OTHER CONDITIONS
Beyerholm[10, 11]	1927	Modified Ekg.	Carotid-radial.	90 persons 15-29 yr. 7.13 30-59 yr. 7.29 60+ yr. 7.82	*Chronic nephritis* with hypertension but without arteriosclerosis —10.21. *Hypertension with arteriosclerosis* —10.44.	Without hypertension —normal for the age of the group—7.52.	*Mitral insufficiency*—no great change in compensated cases. *Arrhythmia perpetua*—no difference in velocity of large and small waves. *Scattered cases* of mediastinal tumor, diabetes, aortic aneurysm and pernicious anemia—no change. *Hyperthyroidism*—usually normal but may be increased.
Ude[12]	1933	Optical	Subclavian-femoral. Femoral-radial. Time difference.	Young controls. 4.33-6.43 (Average 5.64) (20 persons)	High in persons without organic wall changes. 10.2-13.8; average 12.42. (6 cases; 52-81 yr.)	Some increase over normals of the same age. Aortic sclerosis—9.00-15.5; average 11.28. (18 cases; 60-88 yr.) Femoral-radial time difference increased.	*Hypotension*—decreased.
Turner[13, 14]	1927 1934	Helium light	Carotid-radial.		Increased in some cases but variable.	Without hypertension —increased in some cases but variable.	

altered. This problem is of particular interest in connection with the question of increased tonus of the arteries in arterial hypertension, with or without arteriosclerosis.

METHOD

Pulse wave velocities were calculated from pulse wave tracings optically obtained by means of Frank segment capsules, as described by Lauber,[15] Hallock,[2] and others. Pulsations were photographed on a bromide paper moving at approximately 50 mm. per second. The receiving instrument consisted of a shallow wooden cup covered with rubber dam on which, for small arteries, a cork pelote was mounted. It was often necessary to have the subject hold his breath in order to get an even record. Pulsations from the left subclavian, femoral, and dorsalis pedis arteries were usually recorded simultaneously. For each velocity measured, several records of three to six pulse waves each were read by means of a squared glass plate. Measurements were often repeated on a second or third day.

The extensibility of the brachial artery (right carotid-brachial velocity) was measured at different internal effective pressures (the diastolic minus the external pressure applied) by the application of a blood pressure cuff to the upper arm. By the formula of Bramwell, McDowall, and McSwiney[16] the pulse wave velocity and the extensibility of the segment of artery under the cuff were calculated.

Anatomical measurements of the distance between the carotid and brachial arteries were made as described by Bramwell and Hill,[1] and between the subclavian and femoral arteries as described by Lauber.[15] For the subclavian-brachial and the femoral-dorsalis pedis velocities, measurements were made directly on the surface of the body between the centers of the tambours. Satisfactory pulse wave velocities could be obtained only when the distances used were long enough to be measured with reasonable accuracy, as in the subclavian-femoral (aortic) and femoral-dorsalis pedis velocities.

Oscillometric determinations were made on the upper arm and the calf of the leg with a Boulitte modification of the Pachon oscillometer, using the two bags of the cuff as a single bag system. The cuff pressure has been plotted against arbitrary units of oscillation.

The patients studied were recumbent and had rested until their blood pressures were essentially constant. Usually they were in a basal condition, but a few had had breakfast two to three hours before the test. The patients studied included (1) *controls*, with little or no apparent arteriosclerosis, who were recovering from diseases not involving the cardiovascular system; (2) patients with marked *arteriosclerosis*, as indicated by clinical and x-ray examination, but with normal blood pressures; and (3) patients with *arterial hypertension* with little or no arteriosclerosis, whose circulatory state was normal at the time of the test and

whose blood pressures had remained elevated after entry. In our experience patients with normal blood pressure in whom a diagnosis of advanced sclerosis can be made with certainty are not very common. In order to evaluate certain aspects of the problem, we also conducted studies on a number of patients with postural hypotension, aortic regurgitation, hemiplegia, and polycythemia, as well as on hypertensive patients whose blood pressures were low at the time of the tests, although they had previously been high for a considerable period.

RESULTS

I. Pulse Wave Velocity

Averages of pulse wave velocity determinations made on each patient have been summarized in Tables II to VII. The subclavian-brachial or

TABLE II

THE PULSE WAVE VELOCITY IN CONTROL SUBJECTS AND IN PATIENTS WITH ARTERIOSCLEROSIS

NO.	SEX	AGE	DEGREE OF ARTERIOSCLEROSIS	ARTERIAL BLOOD PRESSURE (MM. HG)	PULSE PRESSURE (MM. HG)	PULSE WAVE VELOCITY		
						SUBCLAVIAN-FEMORAL (METERS PER SEC.)	FEMORAL-DORSALIS PEDIS (METERS PER SEC.)	CAROTID-BRACHIAL (METERS PER SEC.)
				Controls				
81	F	18	–	111/63	48	3.42	7.98	4.13
103	M	18	–	124/60	64	4.26	7.86	----
5	F	27	–	105/73	32	5.18	9.62	---
91	M	29	–	107/64	43	5.31	8.46	5.21
9	F	30	–	106/59	47	6.00	8.18	6.18
8	M	31	–	108/63	45	5.30	9.79	5.50
86	M	33	–	118/70	48	4.92	11.14	---
10	F	35	–	104/64	40	5.10	8.69	5.71
26	M	45	±	108/60	48	5.55*	11.11	6.12
22	M	48	–	134/84	50	7.28	9.87	8.85
17	M	49	–	114/70	44	7.07*	9.42	6.48
19	M	52	–	103/65	38	7.73*	9.19	6.42
72	F	56	±	140/76	64	7.06	11.41	7.60
71	M	65	+	109/72	37	7.79	14.30	9.01
59	M	65	+	122/75	47	7.73	12.14	7.06
25	M	73	±	130/66	64	8.33	9.46	6.77
58	M	79	–	127/61	66	10.03	10.68	6.80
				Patients With Arteriosclerosis				
34	M	50	++	114/70	44	6.80	8.75	6.40
35	F	64	++	120/60	60	8.24	12.99	6.09
29	M	65	++++	112/76	36	9.22	10.42	6.45
28	M	70	++++	128/75	53	7.17	10.70	7.36
30	M	70	+++	133/66	67	9.10	12.08	7.82
55	M	74	+++	116/74	42	8.49	11.29	6.30
33	M	75	++	134/63	71	8.96	10.15	8.24
32	M	76	++ or +++	146/68	78	9.76	9.84	6.29
36	M	76	++ or +++	113/64	49	9.65	13.30	7.32

*Carotid-femoral pulse wave velocity.

carotid-brachial pulse wave velocities are based on fewer determinations (one or two) than the other velocities and are therefore somewhat less accurate. The pulse wave velocity may vary by as much as 10 to 15 per cent in the same patient on different days. Pulse wave velocities in young control subjects from eighteen to thirty-five years old (subclavian-femoral 3.42 to 6.00 meters per second, average 4.94; femoral-dorsalis pedis 7.98 to 11.14, average 8.96) agreed with those in the literature in which anatomical measurements were made by the same methods.[12, 17, 18] The data indicate, as Bazett and others have shown, that the pulse wave travels faster in the peripheral arteries than in the aorta.

Changes in Arterial Elasticity With Changes in the Arterial Wall But Without Changes in Blood Pressure.—a. *Age:* The pulse wave velocity of the aorta (subclavian-femoral) increased from approximately 5 meters

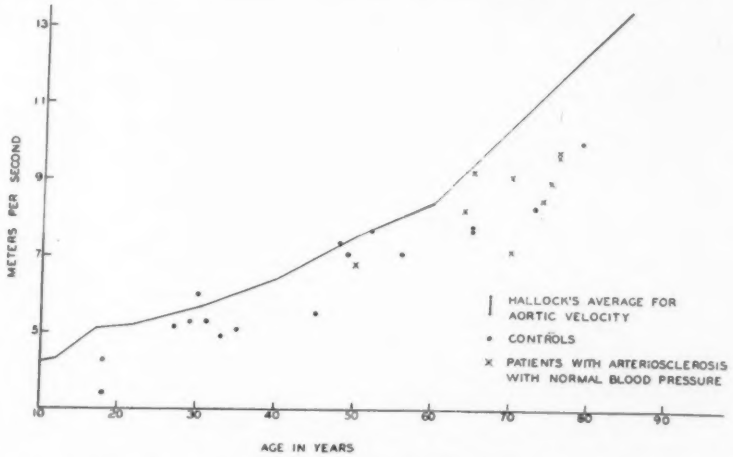

Chart 1.—Relation of the subclavian-femoral (aortic) pulse wave velocity to age in control subjects and in patients with arteriosclerosis.

per second at twenty-five years to 8 or 9 meters at seventy years (Table II and Chart 1). The points fall close to Hallock's[2] average curve for a large series of similar values but are on the average somewhat lower, probably due to the difference in the method of anatomical measurement. The values for the carotid-brachial and femoral-dorsalis pedis velocities (Chart 2) showed a general increase with age, but the spread of points was wider, especially in the femoral-dorsalis pedis velocity. This may be due either to technical difficulties of recording the dorsalis pedis pulsations or to variations in tone in the smaller arteries. To what extent the increase in the velocity with age is due to the blood pressure increase with age is not clear, but the effect of this factor is probably slight. The results agree with morphological findings that

after the early forties there is a progressive loss of elasticity of the arteries, as shown by a thickening and hardening as well as a marked stretching of the walls of the vessels.[19]

b. *Arteriosclerosis:* The results on patients with arteriosclerotic changes in the medium-sized arteries, which were definitely palpable or visible by x-ray, but with normal blood pressures (Table II and Charts 1 and 2), showed that the pulse wave velocities were not abnormally increased but fell directly in line with the controls for the same age group. In fact, Case 28, a patient with extreme Mönckeberg calcification which was easily seen on x-ray, showed rather low pulse wave velocities.

Results in the literature on the effect of arteriosclerotic changes on the pulse wave velocity are variable and hard to evaluate (Table I).[20] Sands[9] has pointed out that tortuosity, especially in the peripheral ves-

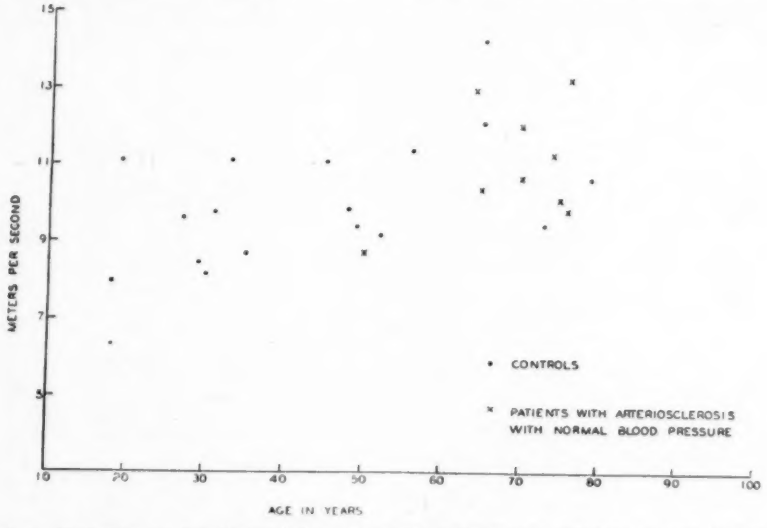

Chart 2.—Relation of the femoral-dorsalis pedis pulse wave velocity to age in control subjects and in patients with arteriosclerosis.

sels, may be an important factor in keeping the pulse wave velocity low in such cases. In Case 28 with low velocities, however, x-rays of the arms and legs showed the arteries to be practically straight. Other factors, such as the diameter of the lumen and the thickness of the arterial wall, may also have a variable influence.

c. *Effect of Preexisting Hypertension:* The arterial velocities of four patients who had had hypertension for some years, but whose blood pressures were lowered to normal levels on account of decompensation or rest in bed, were elevated slightly, if at all, above the values for controls of the same age (Table III). The thickening of the arterial wall, which has been demonstrated by others[19] and which is assumed to be present in the arteries of these patients, is not reflected in arterial elasticity measurements.

TABLE III

THE PULSE WAVE VELOCITY IN PATIENTS WITH PREEXISTING HYPERTENSION

CASE	AGE	DEGREE OF ARTERIOSCLEROSIS	ARTERIAL BLOOD PRESSURE (MM. HG)	PULSE WAVE VELOCITY		
				SUBCLAVIAN-FEMORAL (M./SEC.)	FEMORAL-DORSALIS PEDIS (M./SEC.)	CAROTID-BRACHIAL (M./SEC.)
66	38	∓	109/62	6.48	10.22	7.37
104	41	+	135/90	6.44	9.68	7.25
67	50	+	138/76	7.86	10.93	8.00
68	62	+	130/72	9.74	11.72	8.26

Changes in Arterial Elasticity With Changes in Blood Pressure.—a. *Arterial Hypertension:* In patients with hypertension but with little or no clinical evidence of arteriosclerosis, the pulse wave velocity was increased appreciably over controls of the same age (Table IV). A graphic representation of the relation of the pulse wave velocity to the blood pressure in these patients is complicated by the change in the

TABLE IV

THE PULSE WAVE VELOCITY IN PATIENTS WITH ARTERIAL HYPERTENSION

NO.	SEX	AGE	DEGREE OF ARTERIOSCLEROSIS	ARTERIAL BLOOD PRESSURE (MM. HG)	PULSE PRESSURE (MM. HG)	PULSE WAVE VELOCITY		
						SUBCLAVIAN-FEMORAL (METERS PER SEC.)	FEMORAL-DORSALIS PEDIS (METERS PER SEC.)	CAROTID-BRACHIAL (METERS PER SEC.)
69	F	16	+	182/130	52	7.61	13.57	6.60
50	F	31	−	190/120	70	8.08*	10.62	6.54
92	F	32	+ or ++	220/150	70	11.39*	17.17	9.18
60	M	33	+	148/112	36	13.65	13.28	7.56
51	F	34	−	165/112	53	8.20	10.18	7.04
99	M	37	+	158/110	48	7.36	----	---
49	M	38	−	150/112	38	6.40	11.52	8.20
62	F	38	−	250/145	105	13.02	14.71	7.90
44	F	38	+	160/109	51	12.61	11.58	7.54
100	F	39	−	197/116	81	7.36	----	---
61	F	40	−	190/108	82	9.64	13.08	8.50
73	F	40	+	180/112	68	9.89	13.82	8.55
40	M	44	−	196/120	76	10.72	14.86	6.42
85	M	44	−	202/102	100	10.54	11.32	---
87	F	49	−	214/114	100	14.07	12.99	---
75	M	49	+	192/108	84	10.75	9.28	---
76	F	50	+	206/ 74	132	17.02	14.26	12.02
102	F	52	+	211/103	108	10.13	12.57	---
78	F	53	+ or ++	210/124	86	12.74	13.45	---
47	M	54	+ or ++	160/104	56	9.33	12.26	7.10
70	M	54	+	170/110	60	9.43	12.95	---
48	F	56	+	240/134	106	13.57	13.44	7.58
54	F	58	−	212/110	102	9.92	11.42	6.81
105	F	60	−	208/109	99	15.04*	15.35	10.77
93	F	63	+	180/105	75	11.70	10.32	---
46	F	65	−	190/118	72	13.35	12.48	10.80
45	F	65	+	200/ 85	115	9.48	9.66	6.26
11	F	68	−	175/ 85	90	10.12	8.18	9.20
84	F	69	±	188/ 80	108	15.70	12.39	8.58
53	M	77	±	176/102	74	11.00	13.28	---

*Carotid-femoral pulse wave velocity.

pulse wave velocity with age. If, however, the results for young controls and young hypertensives (ages sixteen to thirty-nine years) are plotted, as well as those for older controls and hypertensives (ages 40 to 77 years), it may be seen that the pulse wave velocity of the aorta in the hypertensive patients ranged considerably above that of controls, although showing a wide spread of points. This was true whether the aortic (subclavian-femoral) velocity was plotted against the systolic, diastolic, mean or pulse pressures (Chart 3). The femoral-dorsalis pedis (Chart 4) and the carotid-brachial velocities were also somewhat increased. The decrease in distensibility due to increase in blood pressure in older patients with hypertension is more apparent in the aorta than in the more muscular peripheral arteries.

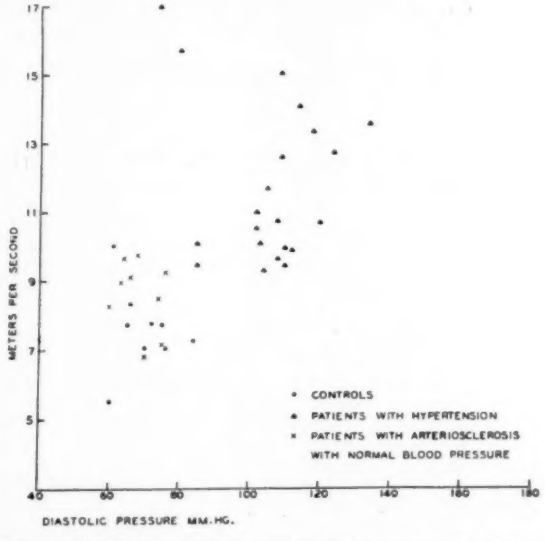

Chart 3.—Relation of subclavian-femoral aortic pulse wave velocity to diastolic blood pressure in older patients (forty to seventy-seven years).

b. *Effect of Vasodilatation:* Since nitrites are known to relax the arterial and arteriolar systems and to lower the blood pressure temporarily, we have given from 2 to 5 grains of sodium nitrite by mouth to ten patients with hypertension and have followed the blood pressure and pulse wave velocities for one to two hours. In all but two patients the systolic blood pressure fell from 20 to 50 mm. Hg as the result of the drug, whereas the diastolic pressure fell to a lesser extent (0 to 20 mm. Hg). Of the eight patients with a blood pressure fall, three showed a fall of over 2 meters per second in the femoral-dorsalis pedis velocity and two others a slight fall. In two cases the subclavian-femoral velocity rose temporarily, and in one case it fell slightly. In the light of these results one cannot consider the fall in systolic pressure as the only significant factor affecting the pulse wave velocity in these cases. Lauber[15] found

a fall in the subclavian-femoral velocity in two cases with a marked fall in blood pressure due to nitroglycerin. Turner and Sodeman,[26] however, mention two instances in which reducing the pressure in hypertensive patients by nitrites actually increased the pulse wave velocity and conclude that changes in arterial tone, largely independent of the blood pressure, may greatly influence the pulse wave velocity in the brachial and radial arteries.

c. *Postural Hypotension:* In order to test the effect of blood pressure, without change in the constitution of the artery, determinations were made on the carotid-brachial and carotid-radial velocities in two cases of postural hypotension. The arm was kept at heart level and measurements were made with the patients lying and standing. Both

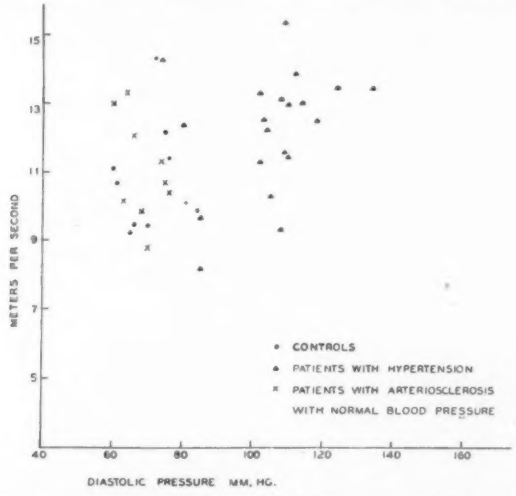

Chart 4.—Relation of femoral-dorsalis pedis pulse wave velocity to diastolic blood pressure in older patients (forty to seventy-seven years).

cases showed a fall in pulse wave velocity accompanying the fall in blood pressure on standing, whereas two controls showed no significant fall in either blood pressure or pulse wave velocity (Table V).

TABLE V

THE PULSE WAVE VELOCITY IN THE HORIZONTAL AND VERTICAL POSITIONS IN CONTROLS AND IN PATIENTS WITH POSTURAL HYPOTENSION

NO.	ARTERIAL BLOOD PRESSURE		PULSE WAVE VELOCITY			
			CAROTID-BRACHIAL		CAROTID-RADIAL	
	LYING (MM. HG)	STANDING (MM. HG)	LYING (M./SEC.)	STANDING (M./SEC.)	LYING (M./SEC.)	STANDING (M./SEC.)
			Controls			
110	102/60	98/58	5.84	5.76	7.44	8.49
111	102/64	102/69	5.25	5.38	6.68	6.54
			Patients With Postural Hypotension			
94	113/75	62/52	9.29	6.31	9.76	7.96
11	168/82	68/56	9.20	5.88	10.08	7.78

d. *Aortic Regurgitation:* We have measured the pulse wave velocities in six cases of aortic regurgitation and present them to demonstrate the effect of a lowered diastolic pressure (Table VI). All but one have a lowered aortic (subclavian-femoral) velocity. The third case, in which the femoral-dorsalis pedis velocity was also measured, showed a low leg velocity, although the systolic pressure in the leg was about 100 mm. Hg higher than that in the arm. The low velocity must be considered

TABLE VI

THE PULSE WAVE VELOCITY IN PATIENTS WITH AORTIC REGURGITATION

NO.	AGE	ARTERIAL BLOOD PRESSURE (MM. HG)	PULSE WAVE VELOCITY		
			SUBCLAVIAN-FEMORAL (M./SEC.)	FEMORAL-DORSALIS PEDIS (M./SEC.)	CAROTID-BRACHIAL (M./SEC.)
96	22	116/56	3.92	---	---
95	25	132/43	4.96	---	---
57	28	160/15	3.70	7.34	---
97	40	101/70	3.92	---	---
98	42	147/32	3.57	---	---
82	58	140/50	6.09	9.69	5.70

an expression of a lowered peripheral resistance and a mean pressure which is not elevated. These results differ somewhat from those of Sands,[9] who concludes that aortic regurgitation without changes in the vessel wall probably has no effect on the pulse wave velocity.

Other Factors Which May Alter the Pulse Wave Velocity.—a. *Hemiplegia:* Owing to the fact that in hemiplegia there is decreased vascular tone on the paralyzed side,[21] the pulse wave velocity was determined on the two sides in five cases of hemiplegia. These cases were measured at least ten days after the hemiplegia took place. The subclavian-femoral values on the two sides checked, as would be expected since the same vessel, the aorta, was chiefly involved. The velocities in the two arms and legs did not vary significantly or consistently. It is apparent (Table VII) that the pulse wave velocity as here measured does not detect any tonus differences on the two sides.

TABLE VII

THE PULSE WAVE VELOCITY* ON THE TWO SIDES IN PATIENTS WITH HEMIPLEGIA

CASE	SUBCLAVIAN OR CAROTID-FEMORAL		FEMORAL-DORSALIS PEDIS		SUBCLAVIAN OR CAROTID-BRACHIAL	
	NORMAL	PARALYZED	NORMAL	PARALYZED	NORMAL	PARALYZED
22	7.28	7.65	9.87	11.10	8.31	7.71
24	6.20	6.10	9.10	10.30	----	7.06
46	13.35	13.86	12.48	12.26	10.80	---
34	6.80	5.98	8.75	8.11	6.40	6.36
23	----	13.47	11.23	11.63	6.38	6.26

*Pulse wave velocities are expressed in meters per second.

b. *Polycythemia:* We had occasion to measure the velocities in two cases of polycythemia. The values for the subclavian-femoral and femoral-dorsalis pedis velocities were low for the age and blood pres-

sure of the patients. In the original formula[2] worked out experimentally for the passage of a pulse wave, the velocity is inversely proportional to the square root of the density of the blood. Although this factor probably is not ordinarily important, a great increase in cells, such as is here represented, may lower the velocity.

II. Arterial Extensibility Curves

Composite extensibility curves for control subjects and patients with hypertension and arteriosclerosis have been plotted in Chart 5. The value at the extreme right on each curve represents the extensibility at the diastolic pressure. As the pressure cuff on the arm was inflated, the effective pressure in the brachial artery was lessened, the pulse wave velocity gradually fell, and the extensibility increased, rising quite sharply as the diastolic pressure was applied. It should be noted that the normal curve plotted from the work of Hemingway, McSwiney, and Allison[22] was obtained from the carotid-radial instead of the carotid-

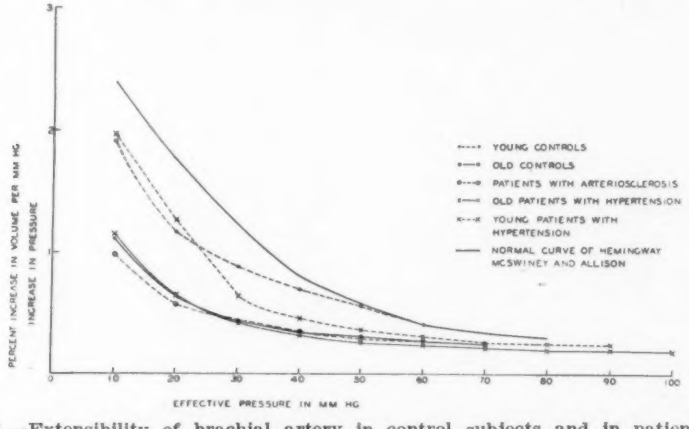
PERCENT INCREASE IN VOLUME PER MM HG INCREASE IN PRESSURE
EFFECTIVE PRESSURE IN MM HG
YOUNG CONTROLS
OLD CONTROLS
PATIENTS WITH ARTERIOSCLEROSIS
OLD PATIENTS WITH HYPERTENSION
YOUNG PATIENTS WITH HYPERTENSION
NORMAL CURVE OF HEMINGWAY MCSWINEY AND ALLISON

Chart 5.—Extensibility of brachial artery in control subjects and in patients with arteriosclerosis and hypertension.

brachial velocity. They also used a wide cuff covering a large part of the arm, instead of an ordinary blood pressure cuff. Our young normals did not include any of the "hyperextensible" individuals mentioned by these workers.

From the curves on the chart it is seen that in agreement with the pulse wave velocity the extensibility of the brachial artery was decreased with age but was not further changed in persons with palpable brachial and radial arteries. In one case with an extreme degree of medial calcification the extensibility curve, although not especially low, was exceedingly flat and did not rise above 0.7 even at zero effective pressure. This probably indicates that the artery was not collapsed, even when a pressure above the diastolic was applied. In older patients with arterial hypertension the extensibility was low, since both the diastolic pressure and the velocity were elevated. When the internal effective pressure was reduced, however, the curve was practically identical with that of

other patients of the same age group without hypertension. The curves of young patients with hypertension were more variable than those of young control subjects and the average curve was a different shape, being somewhat lower along the middle (Chart 5).

III. Oscillometric Curves

Friedlander[23] has pointed out that normally oscillometric readings are not greatly influenced by age. Our normal oscillograms of the upper arm and calf were similar to those shown by Friedlander although the point of maximum oscillation (MOP) was slightly lower. The curve for the hypertensive group, as would be expected, was shifted to the right. In both the upper and the lower extremities the MOP occurred at much higher levels. The unit height of the oscillations was also high. Certain of our cases with marked arteriosclerosis showed relatively low leg curves, but the results varied considerably and seldom fell definitely into the groups described by Friedlander[23] or Finck.[24] In one case of Mönckeberg's sclerosis the arm and leg curves were both very low. The curves on the two sides in patients with hemiplegia did not differ to a greater extent than in normal subjects.

DISCUSSION

The data presented indicate that the changes in the arteries which take place with age are more significant in modifying the pulse wave velocity and extensibility of the arteries than palpable arteriosclerotic changes in the arterial wall. It is apparent that in individual cases of arteriosclerosis the measurements of the pulse wave velocity are not clinically significant as a measure of the degree of arterial change, even when the internal effective pressure is reduced to a constant figure.

The data obtained do not explain the discrepancy that exists in arteriosclerosis between the clinical manifestations and x-ray findings, on the one hand, and the pulse wave velocities, on the other hand. An explanation is suggested, however, by the histological findings, which indicate that atheromatous deposits in the intima and media are usually irregularly scattered and are imbedded in or attached to the otherwise normal structures of the arteries. It appears that as long as the arterial system is not diffusely involved and the bulk of the structure remains normal, there will be no change in pulse velocity. When, on the contrary, the vascular change is diffuse, as occurs in the aging process, alteration in the velocity results, in spite of the fact that clinical and x-ray examinations fail to demonstrate changes. It should also be emphasized that clinical symptomatology of arteriosclerosis depends on the location of focal vascular lesions rather than on the diffuseness of the process. A single cholesterol plaque over the intima of the coronary, cerebral, and certain other arteries will precipitate intense and persistent symptoms and grave alterations of the bodily function, in spite of the fact that the bulk of the arterial system and pulse wave velocity remain

normal. Thus a detailed consideration of the known facts concerning the histopathology and clinical manifestations of arteriosclerosis offers an explanation for the apparent discrepancy existing between the clinical picture of, and the pulse wave velocities in, arteriosclerosis.

As pointed out by Beyerholm,[10] the blood pressure may influence the pulse wave velocity more than the anatomical nature of the vessel walls and the dimensions of the arteries. Conclusions based on observations on normal human beings vary, however, as to whether the velocity is related to the systolic, diastolic, or mean blood pressure.[9, 17, 18, 25, 26] Hallock[2] points out that certain of this work is not valid since the age factor has not been eliminated. High blood pressure mechanically changes the elasticity of the arteries and thus increases the pulse wave velocity. Such a change in the pulse wave velocity, however, is not an indication of a primary organic change in the vascular structure. This is borne

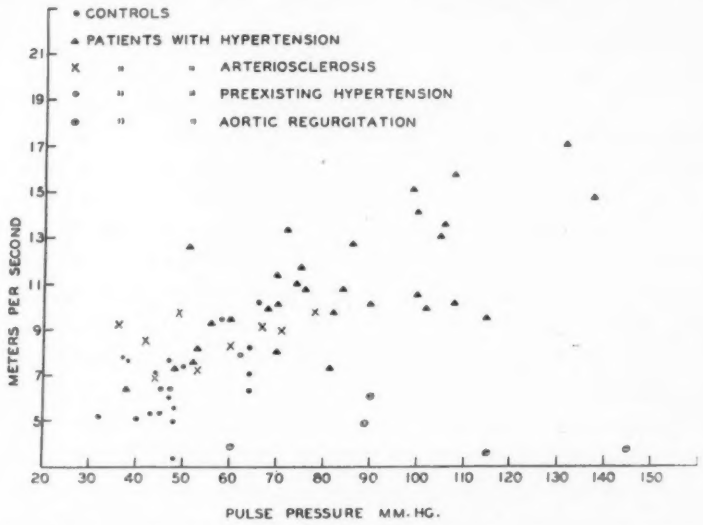

Chart 6.—Relation of subclavian-femoral (aortic) pulse wave velocity to pulse pressure.

out by the fact that following the spontaneous return of the pressure to normal, the values of the pulse wave velocity usually reach normal standards. Furthermore, extensibility curves of the arteries do not indicate changes in the arterial wall, aside from changes in blood pressure.

It is of interest to ascertain as far as possible from the data at hand to what extent pulse pressure is related to the arterial elasticity, as indicated by the pulse wave velocity. In Chart 6 we have plotted in all cases, regardless of age, the aortic (subclavian-femoral) pulse wave velocity against the pulse pressure. In general, as the extensibility decreases (i.e., as the velocity increases, whether due to arterial change or to increased pressure), the pulse pressure increases. The cases of aortic regurgitation form a marked exception. Regardless of the height of the systolic pressure, the velocity remains low, presumably due to the low

diastolic pressure and lowered peripheral resistance. Two patients have been studied who had high systolic pressures associated with normal diastolic pressures, so that the pulse pressures were unusually high (132 to 138 mm. Hg). There was no evidence of aortic insufficiency. These patients had exceedingly high pulse wave velocities, which are represented by the two points at the extreme upper right corner of the chart. This is the type of case in which one would expect to have greatly increased rigidity in the aorta without markedly increased peripheral resistance, as is borne out by velocity measurements.

When the femoral-dorsalis pedis or carotid-brachial velocity is plotted in a similar way, the spread of points is wide, and the relationship to pulse pressure is less apparent. One may expect, therefore, that the conditions in the aorta, which contains considerable elastic tissue, may have more part in determining the pulse pressure than conditions in the smaller, more muscular arteries. The relation of the pulse pressure to arterial elasticity in hypertension will be discussed in the succeeding paper.

SUMMARY

1. The arterial elasticity in normal subjects and in patients with arteriosclerosis, arterial hypertension, and other conditions with alterations in the arterial pressure was estimated from measurements of the subclavian-femoral (aortic), femoral-dorsalis pedis (leg) and carotid or subclavian-brachial (arm) pulse wave velocities, as well as from studies of the arterial extensibility and oscillometric curves.

2. The pulse wave velocity increased with age. Values on patients with clinical and x-ray evidence of marked thickening and calcification of the arteries but with normal blood pressures fell on the curve for controls of the same age group. The extensibility curves of the normal and arteriosclerotic groups were essentially similar. Patients with histories of hypertension of several years' duration, but with normal blood pressures at the time of the test, had essentially the same pulse wave velocities as controls of the same age.

3. Patients with arterial hypertension showed increased pulse wave velocities. The data obtained did not reveal whether this change follows the systolic, diastolic, or pulse pressure most closely. The pulse wave velocity of the aorta was often more affected by blood pressure or pulse pressure changes than was that of the arteries of the extremities.

4. In hemiplegia, tonus differences in the arteries of the two sides were not indicated by differences in the pulse wave velocity.

5. In some cases of arteriosclerosis, oscillometric curves on the calf of the leg were low as compared with those of the upper arm, but the results were quite variable. In patients with arterial hypertension, oscillometric curves were shifted to the right, and the maximal oscillometric phase was often high.

6. While measurements of pulse wave velocities and oscillometric curves give significant information on the physiological aspects of arte-

rial elasticity in health and in disease, no practical conclusions can be drawn from these measurements on an individual case. An apparent discrepancy exists between structural characteristics of the peripheral arteries in arteriosclerosis, as estimated by clinical and x-ray examination, and the results obtained with measurements of the pulse wave velocities. An explanation for this apparent discrepancy is offered.

REFERENCES

1. Bramwell, J. C., and Hill, A. V.: The Velocity of the Pulse Wave in Man, Proc. Roy. Soc. B **93**: 298, 1922.
2. Hallock, P.: Arterial Elasticity in Man in Relation to Age as Evaluated by the Pulse Wave Velocity Method, Arch. Int. Med. **54**: 770, 1934.
3. Friberger, R.: Ueber die Pulswellengeschwindigkeit bei Arterien mit fühlbarer Wandverdickung, Deutsches Arch. f. klin. Med. **107**: 280, 1912.
4. Ruschke: Beitrag z. Lehre von der Fortpflanzungsgeschwindigkeit der Pulswellen bei gesunden und kranken Individuen, Dissert., Jena, 1912.
5. Münzer, E.: Die Fortpflanzungsgeschwindigkeit der Pulswellen in gesunden und krankhaft veränderten Blutgefässen, Verhandl. des deutsch. Kong. inn. Med. **29**: 431, 1912.
6. Silberman: Ueber Pulswellengeschwindigkeit und ihre diagnostische Bedeutung, Zentralbl. f. Herz u. Gefässkrank. **5**: 297, 1913.
7. Laubry, C., Mougeot, A., and Giroux, R.: La vitesse de propagation de l'onde pulsatille artérielle, Arch. d. mal. du coeur **14**: 49, 97, 1921.
8. Bramwell, J. C., and Hill, A. V.: Velocity of Transmission of the Pulse Wave and Elasticity of Arteries, Lancet **1**: 891, 1922.
9. Sands, J.: Studies in Pulse Wave Velocity. III. Pulse Wave Velocity in Pathological Conditions, Am. J. Physiol. **71**: 519, 1924.
10. Beyerholm, O.: Studies of the Velocity of Transmission of the Pulse Wave in Normal Individuals, Acta med. Scandinav. **67**: 203, 1927.
11. Beyerholm, O.: Studies of the Velocity of Transmission of the Pulse Wave in Different Pathological Conditions (principally Arteriosclerosis With and Without Hypertonia, and Heart-Arythmiae), Acta med. Scandinav. **67**: 323, 1927.
12. Ude, H.: Die Beurteilung der Windkesselfunktion der Aorta mit Hilfe der Pulswellengeschwindigkeit, Klin. Wchnschr. **12**: 1484, 1933.
13. Turner, R. H., and Herrmann, G. R.: Pulse Wave Velocity Under Varying Conditions in Normal and Abnormal Human Cardiovascular Systems, J. Clin. Investigation **4**: 430, 1927.
14. Turner, R. H., and Sodeman, W. A.: Observations on Arterial Function, J. Clin. Investigation **13**: 695, 1934.
15. Lauber, H.: Ueber arterielle Blutströmung in normalem und krankhaftem Zustand, Ergebn. inn. Med. u. Kinderh. **44**: 678, 1932.
16. Bramwell, J. C., McDowall, R. J. S., and McSwiney, B. A.: The Variation of Arterial Elasticity With Blood Pressure in Man, Proc. Roy Soc. B **94**: 450, 1922.
17. Bazett, H. C., and Dreyer, N. B.: Measurements of Pulse Wave Velocity, Am. J. Physiol. **63**: 94, 1922.
18. Fulton, J. S., and McSwiney, B. A.: The Pulse Wave Velocity and Extensibility of the Brachial and Radial Artery in Man, J. Physiol. **69**: 386, 1930.
19. Cowdry, E. V.: Arteriosclerosis, New York, The Macmillan Co., 1933, pp. 4 and 518.
20. Wiggers, C. J.: Physical and Physiological Aspects of Arteriosclerosis and Hypertension, Ann. Int. Med. **6**: 12, 1932.
21. Ellis, L. B., and Weiss, Soma: Blood Flow and Edema in Cerebral Hemiplegias, Arch. Neurol. & Psychiat., 1936 (to be published).
22. Hemingway, A., McSwiney, B. A., and Allison, P. R.: The Extensibility of Human Arteries, Quart. J. Med. **21**: 489, 1927.
23. Friedlander, A.: Studies in Oscillometry, AM. HEART J. **9**: 212, 1933.
24. Finck, C.: The Oscillogram, M. J. & Rec. **122**: 411, 1925.
25. Hafkesbring, R., and Ashman, R.: Pulse Wave Velocities in Ninety Subjects, Am. J. Physiol. **100**: 89, 1932.
26. Turner, R. H., and Sodeman, W. A.: Repeated Determinations of Pulse Wave Velocity on Normal Individuals, Proc. Soc. Exper. Biol. & Med. **31**: 831, 1934.

THE RELATION OF ARTERIAL PULSE PRESSURE TO THE HEMODYNAMICS OF ARTERIAL HYPERTENSION*†

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IN PATIENTS with arterial hypertension the pulse pressure varies over an unusually wide range, and high pulse pressure without valvular defect is a common finding. The factors responsible for such a high pulse pressure are not well understood. This investigation was undertaken to ascertain whether certain factors controlling the circulation can be related to the height of the pulse pressure in patients with arterial hypertension.

The chief factors which determine the pulse pressure are necessarily those which influence the height of the systolic and diastolic blood pressures. Wiggers[1] has demonstrated, by means of an artificial circulation machine, the influence of the following factors on the pulse pressure: (1) *Peripheral resistance.* Theoretically an increase in the peripheral resistance alone may be expected to elevate both the systolic and the diastolic blood pressures. Since the outflow of blood at the periphery is relatively less during diastole than during systole, the diastolic pressure is raised to a greater extent than the systolic and the pulse pressure decreases. (2) *Systolic discharge.* Augmented systolic discharge may be expected to increase both the systolic and the diastolic pressures. Since in this condition the outflow of blood is relatively greater during diastole than during systole, the systolic pressure increases more than the diastolic and the pulse pressure increases. Thus increased stroke volume is often associated with an increase in the pulse pressure. (3) *Arterial elasticity.* Decreased arterial elasticity alone elevates the systolic pressure and decreases the diastolic pressure. As Wiggers[1] has pointed out, "This change in systolic pressure is due to the fact that the whole arterial system accommodates less liquid during systolic ejection hence requires a greater pressure to force out the same volume." Owing to the higher systolic pressure the amount of blood flowing away at the periphery is greater during diastole, with the result that the diastolic pressure falls. The mean pressure changes but little.

Under special conditions the heart rate and blood volume must also be considered as affecting the pulse pressure. "At a constant peripheral resistance and a constant volume of ejection a sudden increase in heart rate leads to an . . . increase in systolic and diastolic pressures, the

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diastolic pressure . . . rises more than the systolic, and the pulse pressure decreases.''[1] Increasing the circulating blood volume by infusion of saline or heparinized blood increases the pulse pressure. Wiggers[1] also discusses the bearing of these factors on arterial hypertension.

As has been pointed out by Weiss and Ellis,[2] the influence of these factors in the body is complicated by the fact that a number of regulatory mechanisms are active. Thus in order to obtain a knowledge of the dynamics of the circulation in hypertension, it is necessary to study simultaneously several of the factors which influence the pulse pressure. For this purpose we have made measurements of several of the circulatory functions in hypertensive cases with high, normal, and low pulse pressures.

METHOD

A study of the cardiac output, blood volume, vital capacity, cardiac size, pulse wave velocity, and oscillometric curves has been made on twenty-five cases of arterial hypertension. Patients whose blood pressures had remained elevated after a rest period of several days in the hospital were selected. None of the patients had valvular heart disease or exhibited clinical or laboratory evidence of circulatory failure at the time determinations were made. The majority, fifteen patients, suffered from ''primary'' arterial hypertension without obvious kidney involvement. In the rest various degrees of kidney impairment existed, as was indicated by kidney function tests.

The circulatory measurements were made with the patients in basal condition. The arterial blood pressure was estimated by the Riva Rocci method, using a mercury sphygmomanometer. The acetylene method of Grollman[3] was used for measurement of the cardiac output. The patient was in the sitting position, and two expiratory samples were taken for each determination. The samples were obtained after the sixth and eighth breaths, or at approximately 19 and 25 seconds. Patients were previously trained in the respiratory gymnastics. Care was always taken to adjust the volume of gas rebreathed so that the bag was completely emptied with each respiration. The Benedict-Roth method was used in calculating the oxygen consumption. In all cases duplicate cardiac output determinations were made on the same day. Usually this was repeated one or more times within the next few days. The circulating blood volume was measured according to the technic described by Keith, Rowntree and Geraghty.[4] The mean velocity of the entire circulation was calculated by dividing the circulating blood volume by the cardiac output per minute. Seven-foot x-ray pictures of the heart were taken for cardiac measurements. Pulse wave velocities were obtained optically from pulse curves from the subclavian, femoral, and dorsalis pedis arteries. Anatomical measurements of the length of the arteries were made as described in the preceding paper.[5] The calculation of the cardiac output from the pulse wave velocity was carried out by the method of Broemser and Ranke,[6] which has been more specifically applied to man by Lauber.[7] The results thus obtained were compared with those with the acetylene method. Oscillometric curves were constructed from measurements made on the arm and leg by means of a Pachon oscillometer with a single cuff system, as previously described.[5]

In order to throw light on the problem as to whether or not in vivo the lumen, and hence the volume, of the larger arteries is changed in arterial hypertension, the diameters of the radial and ulnar arteries in an additional group of seven patients with hypertension have been compared with those in seven control subjects. An attempt was also made to measure the arterial lumen in the lower ex-

TABLE I

THE RELATION OF THE PULSE PRESSURE TO THE CARDIAC OUTPUT IN PATIENTS WITH ARTERIAL HYPERTENSION

CASE	AGE	ARTERIAL BLOOD PRESSURE			HEART RATE	OXYGEN CONSUMPTION (C.C. PER MIN.)	CARDIAC OUTPUT BY ACETYLENE METHOD			BLOOD VOLUME		MEAN VELOCITY (SEC.)	VITAL CAPACITY	
		SYSTOLIC (MM. HG)	DIASTOLIC (MM. HG)	PULSE PRESSURE (MM. HG)			(L. PER MIN.)	(L. PER SQ. METER)	(C.C. PER BEAT)	(L.)	(C.C. PER KG.)		(L.)	(L. PER SQ. METER)
156	46	246	128	118	66	262	4.02	2.20	61	5.84	67.7	87	2.10	1.15
155	82	190	79	111	60	228	3.80	2.08	63	5.32	75.5	84	3.60	1.98
100	39	225	121	104	86	221	4.30	2.64	50	4.41	71.9	62	3.20	1.96
101	34	240	140	100	72	266	3.66	2.44	51	----	----	--	2.10	1.40
108	92	181	91	90	64	235	3.78	2.39	59	5.00	87.3	79	----	----
83	59	250	160	90	80	266	3.89	2.43	48	4.63	82.7	72	2.20	1.38
154	81	161	76	85	74	187	3.30	2.11	44	3.74	72.8	68	2.80	1.80
105	60	200	117	83	72	221	3.84	2.38	53	3.88	63.2	61	1.80	1.12
151	69	178	96	82	72	235	4.00	2.75	55	3.71	75.6	56	2.15	1.48
13	57	176	96	80	80	204	3.45	2.18	43	4.50	75.6	78	2.20	1.39
153	59	188	108	80	90	221	3.14	1.92	35	4.02	62.7	77	1.90	1.17
150	57	198	124	74	104	221	2.34	1.36	23	3.81	50.3	98	1.80	1.05
107	40	226	148	78	77	230	3.95	2.35	51	3.88	63.3	59	3.20	1.90
152	28	244	175	69	86	394	5.12	3.15	59	4.94	92.0	58	2.20	1.36
78	51	192	128	64	76	190	2.96	1.82	39	4.45	67.6	90	1.80	1.11
40	44	197	136	61	68	270	4.20	2.56	62	----	----	--	4.20	2.55
92	32	220	162	58	92	238	3.42	2.50	37	4.70	105.5	82	2.90	2.12
51	34	167	109	58	66	171	2.92	1.84	44	4.50	77.3	92	3.20	2.01
47	54	162	107	55	80	266	3.36	2.11	42	6.13	110.3	109	3.80	2.39
99	37	175	125	50	70	272	5.43	2.93	78	6.11	84.0	68	4.20	2.27
106	32	138	95	43	75	278	3.45	1.80	46	5.60	71.2	97	4.00	2.08
44	37	164	122	42	88	218	3.81	2.77	43	4.43	87.8	70	2.60	1.89
60	34	159	121	38	80	235	3.45	2.04	43	5.42	88.9	94	3.10	1.84
69	14	152	118	34	84	232	4.36	3.09	52	3.34	74.2	46	3.00	2.12
12	60	141	110	31	80	225	2.85	1.68	36	4.78	69.2	100	2.30	1.35

tremities, but here the vessels were not clearly visualized. Arteriograms were obtained with the injection of freshly prepared 20 per cent sodium iodide solution under sterile precautions. A 23-gauge hypodermic needle was used for the intra-arterial injection. In order to avoid the influence of pain on the arterial tonus, not only the site of injection, but also the sensory nerves of the forearm were infiltrated with a 2 per cent novocaine solution. All x-ray pictures were taken under standard conditions, the distance between the tube and the forearm being 71 cm. The x-rays were taken about one to two seconds after the beginning of the injection and while it was still in progress. The width of the arterial shadow was estimated to 0.1 mm. with a draftsman's compass on a linear millimeter scale. A certain degree of magnification of the actual diameter occurred on the shadow. Taking into consideration the distance of the x-ray tube and of the artery from the plate, the actual diameter was computed mathematically. It has been estimated that such computation would allow for a maximal possible error of 0.3 mm.

RESULTS

The Relation of Pulse Pressure to Cardiac Output and Systolic Discharge.—Table I and Chart 1 show the relation between the pulse pressure and the cardiac output. The cases have been arranged in the order

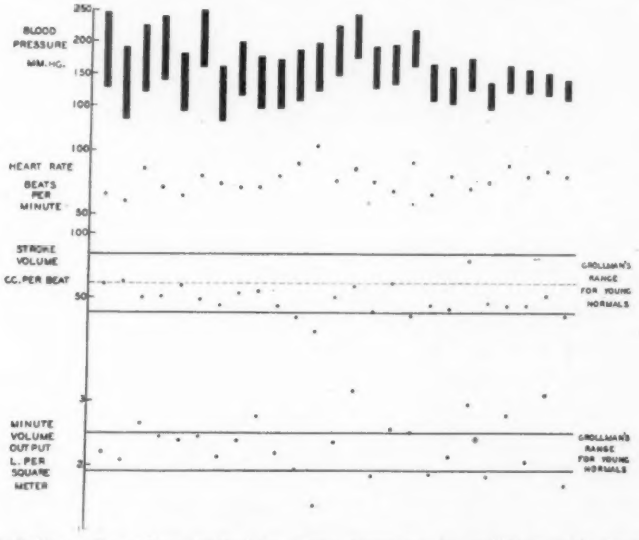

Chart 1.—Relation of cardiac output to pulse pressure in patients with hypertension.

of decreasing pulse pressure. In Chart 1 each vertical column represents one case. The heart rate was normal in all but two of the patients, who had rates of 104 and 92. It may be seen that the stroke and minute output of the heart showed no correlation with the pulse pressure over a range of pulse pressures from 118 to 31 mm. Hg. This is in agreement with observations[2, 8] of the cardiac output determined by the older method of Field, Bock, Gildea, and Lathrop.[9] Thus Burwell and Smith,[8] Weiss and Ellis,[2] and Grassmann and Herzog[10] found normal cardiac outputs in most cases with arterial hypertension. The stroke volumes of our cases (Chart 1) fell within Grollman's[11] range for normal subjects

(38 to 84 c.c. per beat, average 62) in all but four cases, which were slightly low. Our average value, however, was somewhat lower than that obtained by Grollman by the same method. It is of interest that Starr, Doval, Margolies, Shaw, Collins, and Gamble,[12] using an ethyl iodide method, also observed a smaller stroke volume than normal in hypertensive cases. This finding is of significance, for it rules out the theoretical possibility that increased stroke volume is responsible for the elevation of the systolic pressure.

The cardiac output per minute per square meter (Chart 1) showed a wider spread of values than those given by Grollman[11] for young normals (2.2 ± 0.3 liters per square meter). Although some of our patients were older than Grollman's, such a comparison is justified since Lewis and Alving[13] have recently demonstrated that the minute volume output of older age groups remains at the level for adults between twenty and forty years. Of the six cases which varied considerably from Grollman's range, one was an obese woman with a low output (1.36 liters per square meter), whereas four were young persons with high cardiac outputs (2.75 to 3.15 liters). One of the latter may be accounted for by a high basal metabolic rate. In another young patient (fourteen years old) the high value was probably normal for the age of the patient since Starr and his associates[12] have found high outputs for normals below twenty years of age. Thus in only three out of the twenty-five cases studied was the minute cardiac output abnormally high. It should be noted that results may vary as much as 0.4 liter per square meter in the same patient on different days. As in previous studies,[2] our observations fail to reveal any relationship between the systolic blood pressure and the minute and stroke output of the heart (Chart 2).

The Relation of Pulse Pressure to Circulating Blood Volume, Mean Velocity of the Circulation, and Vital Capacity of the Lungs.—The circulating blood volumes ranged between 50 and 110 c.c. per kilogram and were in most cases normal. The volume has been found to be lower in relation to weight in obese persons and relatively high in emaciated subjects.[14, 15] The three most extreme values on Table I appear to be high or low for this reason. A few other cases were slightly below the normal of 72 to 100 c.c. per kilogram.[16] The mean velocity of the entire circulation, calculated by dividing the circulating blood volume by the cardiac output per minute, ranged from 46 to 109 seconds (average 78 seconds) and did not vary with either the pulse pressure or the blood pressure. The vital capacity of the lungs was somewhat lowered in a number of the cases. Such a decrease has been observed before and has been shown to result from pulmonary emphysema, which is frequently present in patients with arterial hypertension. No relation existed between the degree of hypertension or the pulse pressure and the reduced vital capacity.

The Size of the Heart.—The standard diameters of the heart and greater vessels have been tabulated and analyzed. It is of interest that in as many as eight cases (32 per cent) the cardiac shadow was within the limits of normal. In the rest of the cases slight or marked enlargement was present. The size of the cardiac shadow could not be correlated with either the height or the duration of the hypertension. Thus in some patients with severe hypertension of two to three years' duration, the cardiac shadow was within normal limits. We have had a similar experience with a group of patients not included in this series. While it is appreciated that a certain type of ventricular hypertrophy (concentric hypertrophy) may be present with normal cardiac x-ray shadow, the findings suggest that a simple correlation between the height and duration of the arterial hypertension and the size of the heart as obtained from x-ray examination does not exist.

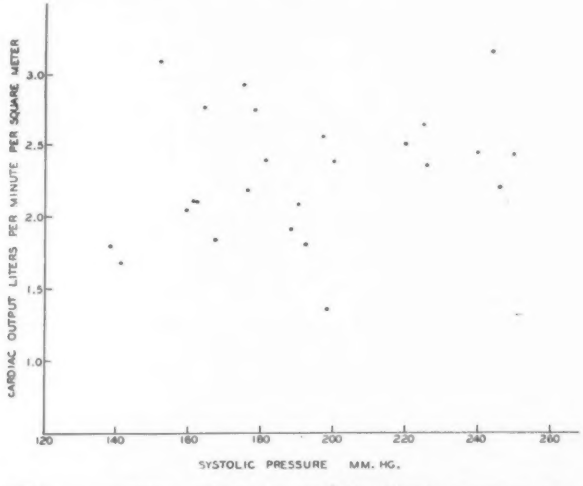

Chart 2.—Relation of cardiac output to systolic blood pressure in patients with hypertension.

The Relation of Pulse Wave Velocity and Oscillometric Measurements to Other Factors Measured.—Table II shows the relationship of pulse pressure to the measurements of arterial elasticity. The change of the pulse wave velocity with the pulse pressure in hypertensive and control patients has been discussed in the preceding paper. In Table II certain of the values there presented have been repeated so that they may be correlated with the cardiac output. In only four cases was there more than slight clinical evidence of arteriosclerosis, and in none of these cases was there marked arterial thickening. It may be seen that the pulse wave velocity bore no relation to the cardiac output. As in the previous work,[5] the pulse wave velocities were high and the cases with the highest pulse wave velocities, i.e., those with the least extensible arteries, tended to be those with the highest pulse pressures (Chart 3). The effect of

TABLE II

THE RELATION OF THE PULSE PRESSURE TO THE PULSE WAVE VELOCITY IN PATIENTS WITH ARTERIAL HYPERTENSION

CASE	AGE	DEGREE OF ARTERIOSCLEROSIS	ARTERIAL BLOOD PRESSURE			HEART RATE	PULSE WAVE VELOCITY		CARDIAC OUTPUT CALCULATED FROM PULSE WAVE VELOCITY		CARDIAC OUTPUT BY ACETYLENE METHOD		OSCILLOMETRIC MEASUREMENTS			
													ARM		LEG	
			SYSTOLIC (M.M. HG)	DIASTOLIC (M.M. HG)	PULSE PRESSURE (M.M. HG)		SUBCLAVIAN-FEMORAL (METERS PER SEC.)	FEMORAL-DORSALIS PEDIS (METERS PER SEC.)	(L. PER SQ. METER)	(C.C. PER BEAT)	(L. PER SQ. METER)	(C.C. PER BEAT)	HEIGHT OF MAX. OSCIL.	MOP (M.M. HG)	HEIGHT OF MAX. OSCIL.	MOP (M.M. HG)
105	60	–	208	109	99	91	15.04	15.35	2.50	58	2.38	53	8	140	15	200
108	92	++	182	91	91	56	11.10	----	4.88	141	2.39	60	17	100	12	100
83	59	++	236	146	90	76	13.84	11.02	3.34	72	2.43	48	--	--	--	--
101	34	++	225	138	87	80	10.94	13.76	2.56	54	2.44	51	17	160	15	180
78	53	+	210	124	86	64	12.74	13.45	3.63	89	1.82	38	12	142	17	165
100	39	–	197	116	81	76	7.36	----	4.15	84	2.64	50	13	115	21	150
13	57	–	157	78	79	72	13.30	14.56	2.60	58	2.18	45	8	90	7	100
107	40	+	234	155	79	72	11.02	----	2.78	66	2.35	50	19	150	21	200
40	44	–	196	120	76	67	10.72	14.86	3.26	80	2.56	62	14	130	16	170
92	32	+	220	150	70	84	11.39*	17.17	2.98	48	2.50	37	--	--	--	--
47	54	++	160	104	56	70	9.33	12.26	2.98	68	2.11	42	10	120	10	130
51	34	–	165	112	53	62	8.20	10.18	2.35	61	1.84	46	7	120	14	150
69	16	+	182	130	52	96	7.61	13.57	3.09	45	3.09	52	6	115	12	120
44	38	+	160	109	51	71	12.14	11.58	2.12	32	2.77	43	12	130	9	175
99	37	+	158	110	48	63	7.36	----	2.66	79	2.93	80	14	130	10	145
106	32	+	136	90	46	70	5.84	----	3.30	89	1.80	47	12	95	12	110
60	33	+	148	112	36	73	----	13.28	1.66	39	2.04	43	--	--	--	--

*Carotid-femoral pulse wave velocity.

changes in the arterial wall itself are difficult to evaluate because of the decrease in distensibility due to the height of the arterial blood pressure.

The oscillometric curves varied considerably in height without reference to the pulse pressure, as has been pointed out in the preceding paper. The point of maximum oscillation (MOP) is somewhat increased above the normal, as might be expected from the height of the blood pressure (Table II). Variation in the height of the oscillations is to be expected from Martin's[17] observations that the oscillations are increased in some hypertensive patients and decreased in others. In cases of essential hypertension he found that the oscillations are often normal or reduced.

The cardiac output calculated from the pulse wave velocity appears in Table II. This calculation has not been found reliable for comparison of different cases. The discrepancy between it and the gaseous determination of the cardiac output is illustrated here.

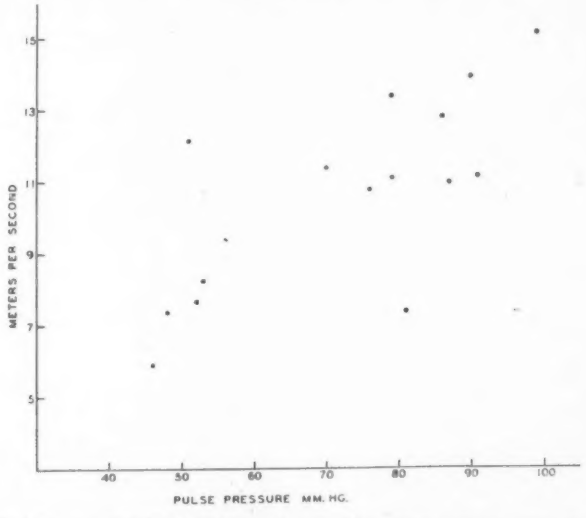

Chart 3.—Relation of subclavian-femoral (aortic) pulse wave velocity to arterial pulse pressure in patients with hypertension.

The Diameter of the Lumen of Radial and Ulnar Arteries in Normal Subjects and in Patients With Arterial Hypertension.—Comparative measurements of the diameter of the radial and ulnar arteries at standard distances from the elbow are presented in Table III. The measurements indicate that no significant variations in the size of the arteries of the forearm can be shown to exist between control subjects with normal blood pressures and patients with a severe degree of arterial hypertension.

DISCUSSION

In 1904 Erlanger and Hooker[18] suggested that the velocity of blood flow could be represented by the product of pulse rate and pulse pres-

TABLE III

DIAMETERS* OF THE LUMINA OF THE RADIAL AND ULNAR ARTERIES IN CONTROL SUBJECTS AND IN PATIENTS WITH HYPERTENSION

STANDARD DISTANCE FROM ELBOW (CM.)	RADIAL ARTERY							ULNAR ARTERY										
	CONTROLS		HYPERTENSIVES					CONTROLS						HYPERTENSIVES					
	1	2	1	2	3	4	5	1	2	3	4	5	6	1	2	3	4	5	6
1									5.3			3.7						3.6	
2									4.0			3.6					4.3	3.5	
3					3.2							3.6							
4		2.3			2.8		2.6		2.8			3.6	3.6			2.4	3.7	2.7	
5		2.1			2.8		2.6	3.2	2.8	3.1		2.5	2.9			2.4	2.9		
6		2.4						3.0	2.8	3.1		2.5				2.4	2.9	2.7	2.6
7		2.1						2.9	2.8	3.1		2.4	2.1			2.3	2.7	2.5	2.6
8		2.1						2.8	2.8	3.1	2.4	2.0	2.1			2.3	2.6	2.5	2.6
9	2.5	2.0				2.5	2.6	2.7	2.8	3.1	2.3	1.9	2.2			2.3	2.4	2.5	2.8
10	2.7					2.5		2.4	2.7	2.8	2.3	1.9				2.1	2.5	2.5	2.9
11	2.8							2.0	2.7	2.8		1.9				2.1	2.5	2.5	2.9
12	2.7							2.1	2.7	2.8		1.7				2.1	2.5	2.3	2.6
13	2.6							2.0	2.7	2.8		1.8		2.7		2.1	2.5	2.3	2.3
14	2.5							2.0		2.8		1.7		2.7		2.1	2.5		
15	2.5							2.0		2.8		1.7		2.7		2.1	2.5		
16	2.0							2.0		2.8		1.7				1.9			
17	2.7							1.9		2.8					2.2	1.9			
18	2.1			3.1				1.9		2.8					2.2				
19	2.1		2.5	3.1				1.9							2.2				
20			2.4	3.1											2.2				
21			2.4	3.1															
22			2.6																

*All measurements are the minimum diameters in millimeters as computed from arteriograms.

sure, assuming that the distensibility of the arterial system remains unchanged. By following the changes in pulse pressure in normal persons on standing and after exercise, Rosen and White[19] have brought evidence to show that the pulse pressure is directly proportional to the output per beat in the same individual under conditions that produce essentially the same diastolic pressure and heart rate. In spite of the limitations of applying such reasoning to the present measurements on different individuals, it is of some interest to calculate the product, pulse rate times pulse pressure, in the cases studied because of the wide range of pulse pressures. In the cases listed in Table I this product is about 7,000 to 8,000 in cases with the highest pulse pressures, and about 2,000 to 3,000 in those with the lowest pulse pressures. Over such a wide range as this no essential change in the cardiac output was observed in patients with arterial hypertension. This is in striking contrast with the state of affairs in other pathological states of the circulation, such as thyrotoxicosis, in which Read[20] has shown that the pulse rate and the systolic pressure increase with increased metabolism but that the diastolic pressure remains constant so that the pulse pressure increases. Harris[21] points out that in contrast to Graves' disease an increase in heart rate in tachycardia due to bacterial toxins, in neurasthenia, or in rapid heart action due to amyl nitrite and atropine is accompanied by a small pulse pressure.

In view of the fact that in the series of cases studied the stroke volume, the cardiac output, the mean velocity of the circulation, and hence the mean capillary flow through tissues were normal, and the aortic valves were competent, the marked variation in the pulse pressure-pulse rate index must find its explanation not in cardiac or circulatory factors but in primary changes in the arteriolar and the arterial vascular systems. That the resistance of the arteriolar system is increased in arterial hypertension is generally accepted. Thus Weiss and Ellis[2, 22] have demonstrated that while the pressure in the skin capillaries is normal, the pressure in the arterioles is considerably increased, at times being more than twice the normal value. In their studies no attempt was made to evaluate the possible rôle of changes in the arteries, in addition to the arteriolar changes. The marked increase in the arteriolar resistance observed should influence primarily the diastolic pressure and to a less extent the systolic pressure. In the types of arterial hypertension associated with a high diastolic pressure and with low, normal, or only moderately elevated pulse pressure, the increased arteriolar resistance can adequately account for the blood pressure levels. This type of arterial pressure is frequently seen in young subjects with acute nephritis. Thus in twenty-five cases with such a diagnosis selected from the records of the Boston City Hospital, the arterial pressure averaged 168/107 mm. Hg.

In the cases in which an unusually high pulse pressure is superimposed on a normal or elevated diastolic pressure, an added factor must be present. We have indicated that theoretically a decrease in either the distensibility or the volume of the arterial system will result in an elevation of the systolic pressure. In the presence of increased arteriolar resistance, such as exists in patients with essential hypertension, relatively less change in arterial elasticity or volume will result in an elevation of the pulse pressure. After due allowance has been made for age and pressure factors, the pulse wave velocity data presented in this and the preceding paper[5] are interpreted as indicating that a primary loss of elasticity in the wall of the aorta was present in only a few instances in which the systolic pressure was high and the diastolic pressure relatively low. On the other hand, the observations reported also indicate that while the method applied was sensitive enough to demonstrate progressive changes with advancing age, it was not adequate to demonstrate other types of alteration in the tonus and constitution of the larger arteries.[5] Thus one can only claim that in the majority of patients with arterial hypertension the degenerative changes which normally occur with advancing age are not further accentuated and that such change in the arterial system is not usually the factor responsible for the development of high pulse pressure.

Hochrein[23] has claimed that there is a loss of elasticity in the aortas of patients with hypertension, and he believes that this plays a primary rôle in the elevation of the blood pressure. His conclusion was reached through post-mortem studies of the elastic properties of the aorta; hence there is a possibility that the changes may have been the result rather than the cause of the hypertension. That changes in the arteries alone, however, can lead to an elevation of the systolic pressure is demonstrated in patients with diffuse sclerosis of the aorta and with complete heart-block. In these conditions a high systolic pressure and a normal or decreased diastolic pressure frequently exist. Thus in a study of the hemodynamics of complete heart-block Ellis and Weiss[24, 25] have observed high systolic pressures in elderly patients, while young patients with an equal increase in the stroke volume exhibited normal pulse pressures. This finding suggests that the normally elastic arterial system possesses a reserve capacity which is able to accommodate even a greatly increased stroke volume with little or no elevation of the systolic pressure. Just as in complete heart-block a markedly increased stroke volume can elevate the systolic pressure in the presence of decreased elasticity of an arterial system, so a priori a normal stroke volume should result in an increase in the systolic pressure if the arterial system is conspicuously narrow. In view of the fact that measurements of the internal diameters of the radial and ulnar arteries have failed to indicate an alteration of the diameters of these vessels, and similarly that the lumina of the arteries of the eyegrounds are usually not narrowed in primary

hypertension, there is basis for the claim that narrowing of the large arteries usually plays no primary rôle in the elevation of the systolic blood pressure.

From the previous discussion it follows that the marked variations in the levels of the systolic and diastolic pressures in hypertension depend on certain types of changes in physical properties of the arterial and arteriolar systems. Extravascular factors, such as cardiac and hemodynamic elements, as a rule do not play a primary etiological rôle in arterial hypertension. The fact that in the majority of patients the elevation of the systolic pressure is relatively greater than that of the diastolic pressure indicates that usually both the arteries and the arterioles are involved in the changes. In various pathological states associated with elevated arterial pressure, however, one or the other of these vessels may be predominantly involved. Thus the character of the blood pressure in patients with acute nephritis and toxemia of pregnancy points to the arteriolar system as the predominant factor. In hypertension associated with the senile type of arteriosclerosis, on the other hand, changes in the arterial system are mainly responsible for the altered circulatory state. It is of particular significance from a point of view of homeostasis that circulatory changes resulting from alterations in the arterial and arteriolar systems are such that the resulting mean flow of the blood through the capillary system remains normal.

The exact nature of the arterial and arteriolar changes in hypertension is not well understood. From what is known at present, however, it is certain that both reversible (functional) and irreversible (organic) processes can take part. With bed rest the systolic and diastolic pressures of patients with severe hypertension frequently return to normal without any change in the efficiency of the circulation. This indicates that, in at least one large group of patients, the alterations in the physical properties of the arterial and arteriolar systems are not permanent, as are the changes with age, but are reversible. Reversible change in the arterial system is also suggested by the work of MacWilliam,[26] who has shown that the arteries immediately after death are capable of considerable alteration in tonus, with resulting change in their elastic properties. Evidence recently obtained in this laboratory[27] also favors the concept that the hypertonus of the arterioles is also largely reversible and that it may be independent of the vasomotor system.

SUMMARY

1. In order to ascertain the relation of the pulse pressure to the hemodynamics of arterial hypertension, determinations of the cardiac output, blood volume, and pulse wave velocity, and oscillometric measurements have been made in twenty-five cases of hypertension with high, normal and low pulse pressures. In addition, measurements of arteriograms of

the radial and ulnar arteries have been compared in seven control subjects and seven patients with arterial hypertension.

2. The cardiac stroke volume and minute volume output bore no relationship to the pulse pressure in arterial hypertension. In spite of the high pulse pressure, the heart rate, stroke volume, minute volume output of the heart, and the blood volume were found to be essentially normal. The pulse wave velocity was high, and it bore a certain relation to the pulse pressure. The lumina of the radial and ulnar arteries were of the same width as in the control subjects.

3. The results of the investigation are interpreted as indicating that the high systolic pressure of hypertension depends in part on alterations in the physical state of the aorta and arteries. As judged from the clinical behavior of the blood pressure, the nature of the change within the arterial wall is not uniform. In the group studied the change was of a different nature from that found as a result of aging processes.

4. There are changes in the physical properties of both the arterial and arteriolar systems in arterial hypertension. The relative degree of involvement of the arteries and arterioles can vary considerably in various types of arterial hypertension. The exact nature of the changes in the arterial and arteriolar systems is not known.

5. In arterial hypertension there is a remarkable homeostatic adaptation of the heart and of the circulation to the primary changes in arterial and arteriolar systems.

REFERENCES

1. Wiggers, C. J.: Physiology in Health and Disease, Philadelphia, 1934, Lea & Febiger, pp. 598-601; also Ann. Int. Med. **6:** 12, 1932.
2. Weiss, Soma, and Ellis, L. B.: The Quantitative Aspects and Dynamics of the Circulatory Mechanism in Arterial Hypertension, AM. HEART J. **5:** 448, 1930.
3. Grollman, A.: The Determination of the Cardiac Output of Man by the Use of Acetylene, Am. J. Physiol. **88:** 432, 1929.
4. Keith, N. M., Rowntree, L. G., and Geraghty, I. T.: A Method for the Determination of Plasma and Blood Volume, Arch. Int. Med. **16:** 547, 1915.
5. Haynes, F. W., Ellis, L. B., and Weiss, Soma: Pulse Wave Velocity and Arterial Elasticity in Arterial Hypertension, Arteriosclerosis and Related Conditions, AM. HEART J. **11:** 385, 1936.
6. Broemser, P., and Ranke, O. F.: Ueber die Messung des Schlagvolumens des Herzens auf unblutigem Weg, Ztschr. f. Biol. **90:** 467, 1930.
7. Lauber, H.: Ueber arterielle Blutströmung in normalem und krankhaftem Zustand, Ergebn. inn. Med. u. Kinderh. **44:** 678, 1932.
8. Burwell, C. S., and Smith, W. C.: The Output of the Heart in Patients With Abnormal Blood Pressures, J. Clin. Investigation **7:** 1, 1929.
9. Field, H., Jr., Bock, A. V., Gildea, E. F., and Lathrop, F. L.: The Rate of the Circulation of the Blood in Normal Resting Individuals, J. Clin. Investigation **1:** 65, 1924.
10. Grassmann, W., and Herzog, F.: Die Wirkung von Digitalis (Strophanthin) auf das Minuten- und Schlagvolumen des Herzkranken, Arch. f. exper. Path. u. Pharmakol. **163:** 97, 1931.
11. Grollman, A.: The Cardiac Output of Man in Health and Disease, Springfield, Ill., 1932, Charles C. Thomas, p. 87.
12. Starr, I., Doval, J. S., Margolies, A., Shaw, R., Collins, L. H., and Gamble, C. J.: Studies of the Heart and Circulation in Disease: Estimations of Basal Cardiac Output, Metabolism, Heart Size, and Blood Pressure in 235 Subjects, J. Clin. Investigation **13:** 561, 1934.

13. Lewis, W. H., and Alving, A. S.: Changes in the Minute Volume Output of the Heart and Urea Clearance in Relation to Age, J. Clin. Investigation **13**: 691, 1934.
14. Brown, G. E., and Roth, G. M.: Volume and Composition of the Blood in Addison's Disease, Am. J. M. Sc. **169**: 47, 1925.
15. Mendershausen, A.: Blutmengenbestimmungen mit der Kongorotmethode, Ztschr. f. klin. Med. **97**: 468, 1923.
16. Peters, J. P., and Van Slyke, D. D.: Quantitative Clinical Chemistry, Vol. I. Interpretations, Baltimore, 1931, Williams & Wilkins Co., p. 725.
17. Martin, J.: Essai sur l'oscillométrie dans l'hypertension artérielle, Paris, 1932, Jouve & Cie.
18. Erlanger, J., and Hooker, D. R.: An Experimental Study of Blood-pressure and of Pulse-pressure in Man, Johns Hopkins Hosp. Rep. **12**: 145, 1904.
19. Rosen, I. T., and White, H. L.: The Relation of Pulse Pressure to Stroke Volume, Am. J. Physiol. **78**: 168, 1926.
20. Read, J. M.: A Clinical Interpretation of Pulse Pressure, AM. HEART J. **2**: 541, 1927.
21. Harris, I.: The Pulse Pressure in Exophthalmic Goitre, Brit. M. J. **1**: 630, 1923.
22. Ellis, L. B., and Weiss, Soma: The Measurement of Capillary Pressure Under Natural Conditions and After Arteriolar Dilatation; in Normal Subjects and in Patients With Arterial Hypertension and With Arteriosclerosis, J. Clin. Investigation **8**: 47, 1929.
23. Hochrein, M.: Ueber den Kreislaufmechanismus bei der Hypertension, Habilitationsschrift, Leipzig, 1928.
24. Ellis, L. B., and Weiss, Soma: Studies in Complete Heart Block. I. The Cardiac Output and the Peripheral Circulatory Mechanism, Am. J. M. Sc. **182**: 195, 1931.
25. Ellis, L. B.: Studies in Complete Heart Block. II. A Clinical Analysis of 43 Cases, Am. J. M. Sc. **183**: 225, 1932.
26. MacWilliam, J. A.: On the Properties of the Arterial and Venous Walls, Proc. Roy. Soc. **70**: 109, 1902.
27. Prinzmetal, M., and Wilson, C.: The Nature of the Peripheral Resistance in Arterial Hypertension With Special Reference to the Vasomotor System, J. Clin. Investigation **15**: 63, 1936.

SOME CASES OF SLOW PULSE ASSOCIATED WITH ELECTROCARDIOGRAPHIC CHANGES IN CARDIAC PATIENTS AFTER MAXIMAL WORK ON THE KROGH ERGOMETER

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IN WORKING out a cardiac functional test with Krogh's bicycle ergometer we encountered some peculiar pulse curves which will presumably be of interest to the clinician who tries to estimate the functional capacity of the heart by examination of the pulse during or after exercise. The remarkable feature of these pulse curves is that immediately after maximal work on the ergometer the pulse rate falls off temporarily to a point considerably below the resting value. This transitory phenomenon is accompanied by transitory massive changes in the electrocardiogram. As we have observed this pulse phenomenon only in connection with unquestionable pathological working electrocardiograms, we are inclined to attribute some pathological significance to its appearance.

Before mentioning these curves we shall outline briefly the technic we have employed. The patients are examined fasting, after a suitable rest on a couch in the laboratory. The resting pulse rate (base line) is determined electrocardiographically after the patient has been sitting relaxed on the bicycle for five minutes. The work is performed on the Krogh bicycle ergometer, with a riding tempo constant by metronome (30 rotations per minute), and with increasing load, three minutes' work with each load, the change of load taking place *during* the ride. With some experience this change of load is easily made in a few seconds. After reaching the maximal amount of work the patient is instructed to place his feet on the footboards of the bicycle and sit perfectly relaxed. The pulse rate is measured electrocardiographically every three minutes during the work, in such a way that the counting of the pulse is always made in the same fraction of the minute, making all the counts directly comparable. In the afterperiod the pulse is counted every minute until it is found to remain constant for four consecutive minutes. The pulse count is made with a transportable Boulitte electrocardiograph. The muscular unrest during the work is moderated by the insertion of a small condensator in the chest lead. Orientating experiments have shown that the results obtained with such a continually increasing load during the work give the same information as do single tests in which the patient rides the bicycle with one load at a time and

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with a period of complete rest after each test; this technic saves a good deal of time. This method gives a pulse value for each amount of work besides information about the course of the pulse curve for about ten minutes after the work. Each patient is submitted to the ergometer test at least three times (on three consecutive days).

The present studies have given us the impression that the working pulse as it appears with a given amount of work is a value that can easily be reproduced from day to day under the given experimental conditions. In the not particularly frequent instances in which a distinct training effect could be made out, the experiments were prolonged until it was practicable to obtain conformable results allowing of graphical smoothing.

The working electrocardiograms are taken (by Kaj Larsen) with an amplifier apparatus furnished by Siemens-Halske, constructed by Professor Warburg, and tried out by Warburg and Larsen.[1] As it was

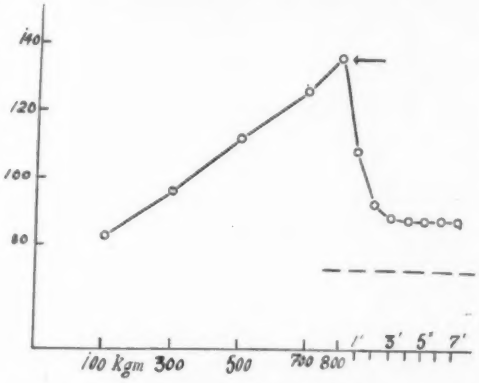

Fig. 1.—Horizontal turn of pulse curve after work in normal persons.

--------- Resting pulse
o———o Pulse
←——— End of work

found impracticable with the patient sitting on the ergometer to obtain the state of muscular rest required for good electrocardiography with *extremity* leads, we have instead employed leads from the wall of the chest, as suggested by Groedel,[2] partly from the xiphoid process, partly from the left axilla at a level with and a little lateral to the apex of the heart. The electrodes were small metal-felt-saline electrodes, fixed with a rubber band. In the following, for practical reasons the lead from the xiphoid process will be designated as Lead *d* (dexter), and the lead from the left axilla as Lead *s* (sinister). But whether the two leads, as Groedel thinks, represent the potential changes in the right and left ventricles, respectively, is a question we shall leave open for the present. In order to eliminate the factor of uncertainty that might result from a limited knowledge of electrocardiograms from the thoracic leads, in one series of tests we have placed the patient in an easy-chair alongside

the ergometer before and after the work and then have taken in immediate succession electrocardiograms from the ordinary leads and from thoracic leads.

As is well known, the pulse curve falls at once when the work is discontinued. As a rule, however, this fall of the pulse rate goes on only for a few minutes, when the curve makes an abrupt turn to a horizontal level and becomes steady somewhat above the level of the resting pulse. This turn of the pulse curve is very pronounced and easy to recognize (Fig. 1).

With a view to the findings and comments in the following we wish here to emphasize explicitly that in normal persons we have never seen the pulse curve fall below the level of the resting pulse (base line) in the period of about ten minutes we employ for observation. After this period the curve falls off but exceedingly slowly, and it may take several hours before it reaches the base line. For practical reasons, we have taken no interest at all in this part of the pulse curve; as already mentioned, we have ceased counting the pulse as soon as we have obtained constant readings for four minutes in succession.

Also the comparatively few controls we have examined show a rather uniform appearance of thoracic electrocardiograms before and after work (Fig. 2). As we are interested here particularly in the behavior of the S-T interval and T-wave, it will be appropriate to describe these features briefly. During rest both $S\text{-}T_d$ and $S\text{-}T_s$ are most often a little above the isoelectric line, and both T-waves are distinctly positive. Immediately after the work the S-T intervals are seen to approach or reach the isoelectric line, without going below this level. Immediately after work the T-waves may be a little higher, of the same height, or a little lower than before work, but they increase in every case during the first minute of work, reaching a maximum in one to two minutes; after this they decrease, in most cases reaching in four to six minutes a lower level than before the work, and then they slowly increase toward their original height. In no case in normal persons were the T-waves isoelectric, much less negative.

Up to the present we have examined 50 patients in the Departments A, B, and P of the Rigshospital, including 25 normal (i.e., as far as the heart is concerned) and 25 cardiac patients (mostly cases of myocardial degeneration). The material is gathered in order to obtain average values for the pulse frequency in normal persons and patients during work, but it is yet all too small to allow of any comprehensive account of the results. The cases presented in this paper, however, are so characteristic, we think, that it is reasonable to give a preliminary account of them now, regardless of the possible frequency of their occurrence.

CASE 1.—C. C., male, fifty-eight years old. Past history was negative as to rheumatic fever, diphtheria, and scarlet fever. Ten years ago he had an attack of mumps associated with orchitis. For the last seven months the patient had com-

plained of pain of an oppressive character in the chest, localized to the manubrium and provoked by rapid movements and heavy meals but not by exposure to cold. The pains were radiating, at first to the left arm, then to the right arm and to the back, also down in the legs. The pains were not accompanied by anxiety or dyspnea and subsided after rest. There was typical "second wind" and often attacks of profuse sweating. There had never been any dyspnea, palpitation of the heart, or edema. The patient had worried a great deal during the past year.

Physical Examination.—The patient appeared healthy, but a little obese. Heart: Ictus in the fifth intercostal space, within the midclavicular line; the sounds were

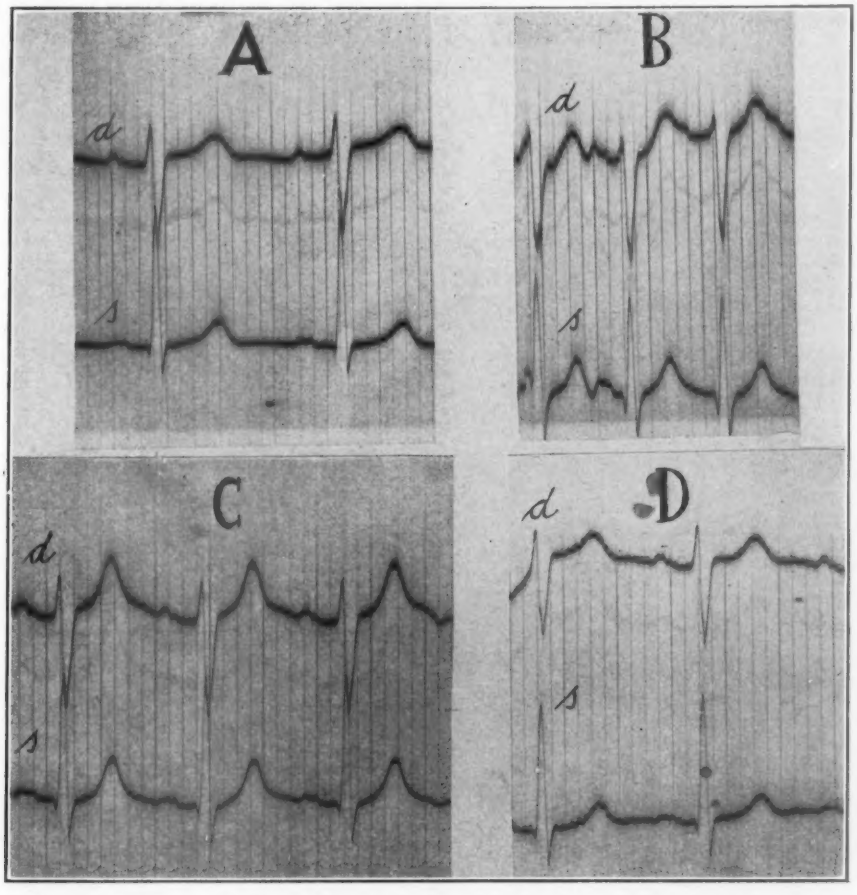

Fig. 2.—Working electrocardiograms of normal persons: *A*, thoracic lead before work; *B*, 10 seconds after cessation of work; *C*, 2 minutes after cessation of work; *D*, 6 minutes after work. (Time marker, 0.05 second; 1 millivolt—20 mm.)

clear, $A_2 > P_2$; the second sound was weak over the aorta as well as over the pulmonary artery. No demonstrable stasis in the lungs, liver, or legs.

Special Examinations.—Wassermann and Kahn reactions were negative. Hemoglobin content was 106 per cent; sedimentation test (one hour), 7 mm. The urine showed no abnormalities. Blood pressure readings were 140/90, 145/85, 142/80. Vital capacity, 4.7 liters. Roentgenography: Heart measured 15×32×8 cm., no definite abnormalities. Abdomen: Rather large hiatus hernia. Electrocardiography: Left preponderance. Registration of heart sounds: No abnormalities.

Summary of Positive Findings.—Dilatation of the aorta, preponderance of the left side of the heart, diaphragmatic hernia.

Diagnosis.—Angina pectoris, aortic dilatation, hypertrophy of the left ventricle, and diaphragmatic hernia.

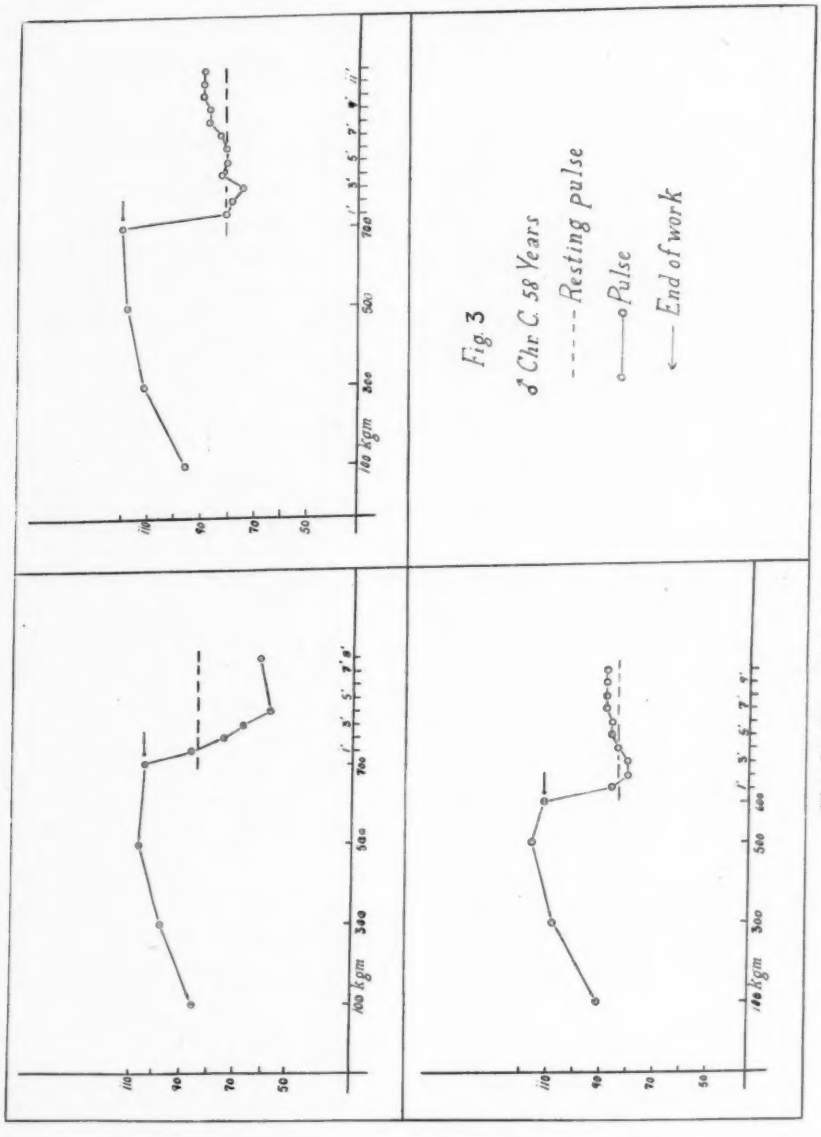

Fig. 3.—Ergometer tests on May 14, 16, and 18.

Ergometer Test (Fig. 3).—The maximal output of work was 700 kilogram-meters per minute. Even with an output of 600 kg-m the patient began to have pain back of the manubrium. After cessation of work the pulse curve falls off in three minutes to a minimum at a vary-

ing distance below the base line; then it rises slowly. The patient was very exhausted after the first test which had to be discontinued on that account.

Working Electrocardiograms (Fig. 4).—Four ergometer tests showed pronounced electrocardiographic changes, consisting in a pronounced depression of S-T_s and inversion of T_s. In one experiment, in which the patient rode 100-300-500-600 kg-m and in which electrocardiograms were taken during the bicycling, the electrocardiographic changes were found to begin at 500 kg-m and to be very pronounced at 600 kg-m. At 500 kg-m the patient began to have pain in the chest, and at the same time the pulse rate ceased rising (500 kg-m. with a pulse rate of 119, 600

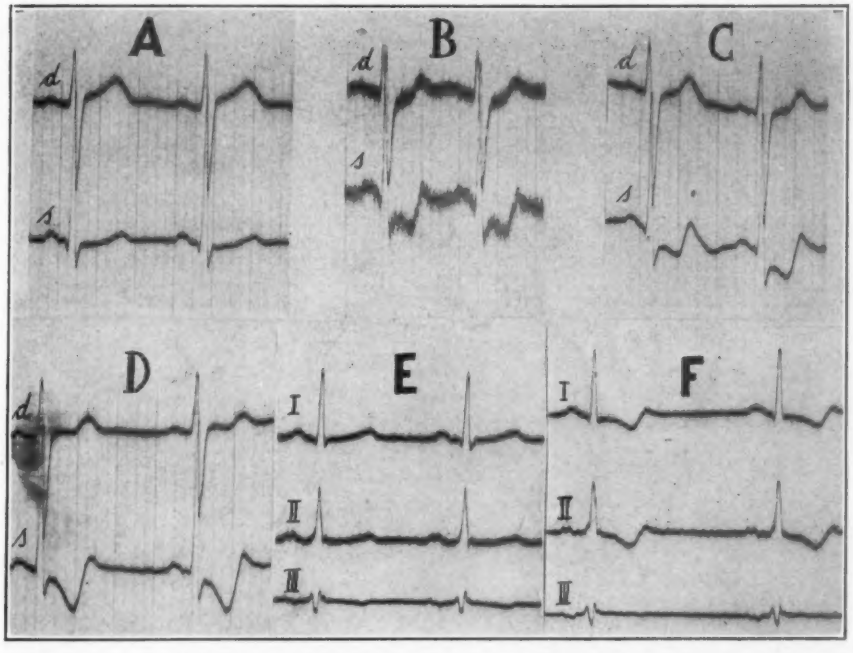

Fig. 4.—C. C. Working electrocardiogram: *A*, thoracic lead before work; *B*, during bicycling with a load of 600 kg-m; *C*, 5 seconds after cessation of work; *D*, 2 minutes after cessation of work; *E*, extremity lead before work; *F*, extremity lead 2 minutes after work. (Time marker, 0.05 second; 1 millivolt—20 mm.).

kg-m. with a pulse rate of 120). The depression of S-T_s was greatest immediately after the cessation of work, and then it diminished gradually. The inversion of T_s, on the other hand, kept getting more pronounced and reached its maximum in from one and one-half to three minutes; then it subsided. Still, it took nine minutes after cessation of work before the electrocardiogram looked fairly like the prework record. In Lead *d* the changes were only slight. S-T_d prior to the work was seen to be somewhat above the isoelectric line; immediately after cessation of work this interval was seen to have become isoelectric, and T_d was seen at the same time to have been lowered a little bit. These

changes had disappeared six minutes later, and nine and twelve minutes after work T_d was somewhat higher than before work. In Fig. 4 *E* and *F* the changes here described in the thoracic lead correspond to a considerable depression of S-T_1 and S-T_2 and to the inversion of T_1 and T_2. According to our present experiments, the absence of electrocardiographic changes in Lead III is quite in keeping with the fact that in the thoracic lead the changes are pronounced only in Lead *s*.

CASE 2.—J. P. N., male, fifty-two years old. Past history was negative as to rheumatic fever, diphtheria, and scarlet fever. The patient claimed he had always been well until December 2, 1933, when suddenly while working he had an attack of severe pain back of the sternum, radiating out into both arms and around to the back, and being accompanied by marked dyspnea, anxiety, and sweating. The attack lasted between one and two hours. He had to quit work and go home, where his doctor gave him morphine, which relieved him. He was then hospitalized for two months. He has since had frequent attacks of constricting precordial pains, radiating in various directions (at present to the right ear only) and, in the beginning, accompanied by dyspnea and anxiety. The attacks have diminished in intensity, but they are elicited very easily by walking or by plentiful meals, and sometimes they appear also during rest. The attacks last, as a rule, from five to ten minutes and subside when the patient stands still.

Physical Examination.—There was slight obesity and, on admission, congestion of the face, with a cyanotic hue. There was no resting dyspnea, no jaundice. Auscultation of the heart revealed normal findings. There was no demonstrable congestion of the lungs or liver. A suggestion of edema was noted about the ankles.

Special Examinations.—Wassermann and Kahn reactions were negative. Blood pressure readings were 175/105, 160/95, 155/95. Sedimentation test (one hour), 42 mm., hemoglobin, 98 per cent. The urine showed no abnormalities. Roentgenography: Heart measured 15×31 cm.; the shape was suggestive of dilatation of the left half of the heart. No dilatation of the aorta (7 cm.). Electrocardiography: Left preponderance; low T_1, isoelectric T_2. Vital capacity, 3.9 liters. Registration of heart sounds: No abnormalities.

Summary of Positive Findings.—Cyanosis, edema about the ankles, roentgenologically demonstrable changes in the size and shape of the heart, preponderance of the left side of the heart, low T_1, and isoelectric T_2.

Diagnosis.—Coronary sclerosis, sequelae of coronary thrombosis.

Ergometer Test (Fig. 5).—As in Case 1, the pulse curve is distinctly negative, i.e., within a few minutes after cessation of work the pulse curve falls off to a point below the base line, and then it rises again. Also this patient complained of anginoid pain at the end of the work.

Working Electrocardiograms (Fig. 6).—Four ergometer tests show pronounced changes after the work characterized by depression of both S-T intervals and by a transitory total inversion of both T-waves. After nine to ten minutes the electrocardiogram appears normal once more.

CASE 3.—R. H., male, fifty years old, had an attack of myopathy in the right pectoralis region two years ago. Otherwise the patient gave a past history of good health. During the last year he had been troubled with attacks of retrosternal pain radiating out to the left arm. More recently these attacks increased in intensity and frequency, making their appearance in the night during rest as well as in the day during work. They were not associated with any particular anxiety, and

the pain appeared never to reach the intensity which is most common in attacks of anginoid pain. Apart from this, the patient had never shown any sign of organic heart lesion. Lately, he had many attacks every day. The pains yielded readily to nitroglycerin.

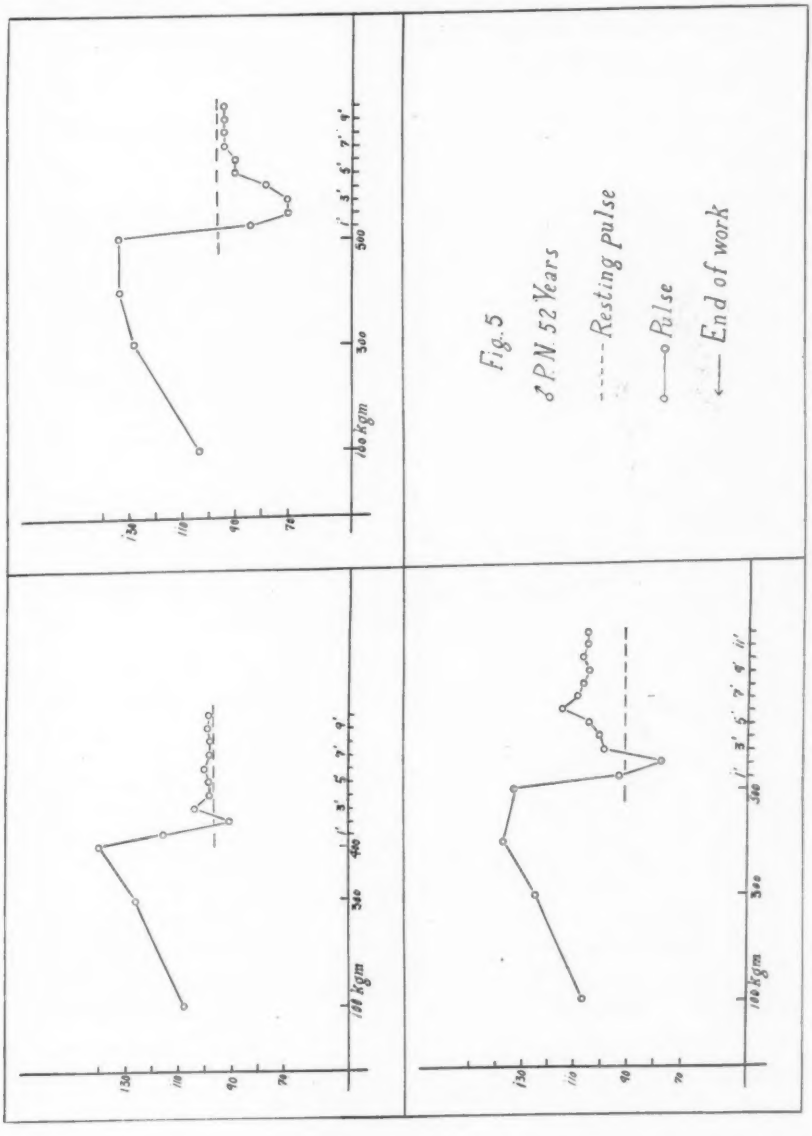

Fig. 5.—Ergometer tests on April 24, 25, and 26.

Physical Examination.—Slight obesity. On percussion the lung borders are found to be at ribs 7, 9, and 11. The breath sounds are vesicular, without abnormal sounds. Auscultation of the heart: Heart lung-covered; heart sounds faint, clear; action regular. No demonstrable congestion of the lungs, liver or legs. No demonstrable myopathic processes in the pectoralis.

Special Examinations.—Wassermann and Kahn tests were negative. Sedimentation test (one hour), 4 mm.; blood pressure readings were 130/60, 130/70, 120/70;

hemoglobin, 89 per cent. The urine showed no abnormalities. Roentgenography of the heart: Normal form and size (hardly 15 cm. against 29.5). No increase in the width of the shadow of the vessels. No sign of aortic arteriosclerosis. Moderate arteriosclerosis in the right leg and forearm. Electrocardiography: Q_3 is greater than 25 per cent of the greatest wave present. Registration of heart sounds: No abnormalities.

Summary of Positive Findings.—Emphysema, large Q_3, and peripheral arteriosclerosis.

Diagnosis.—Emphysema of the lungs (slight degree), observation for myocardial degeneration, angina pectoris, arteriosclerosis.

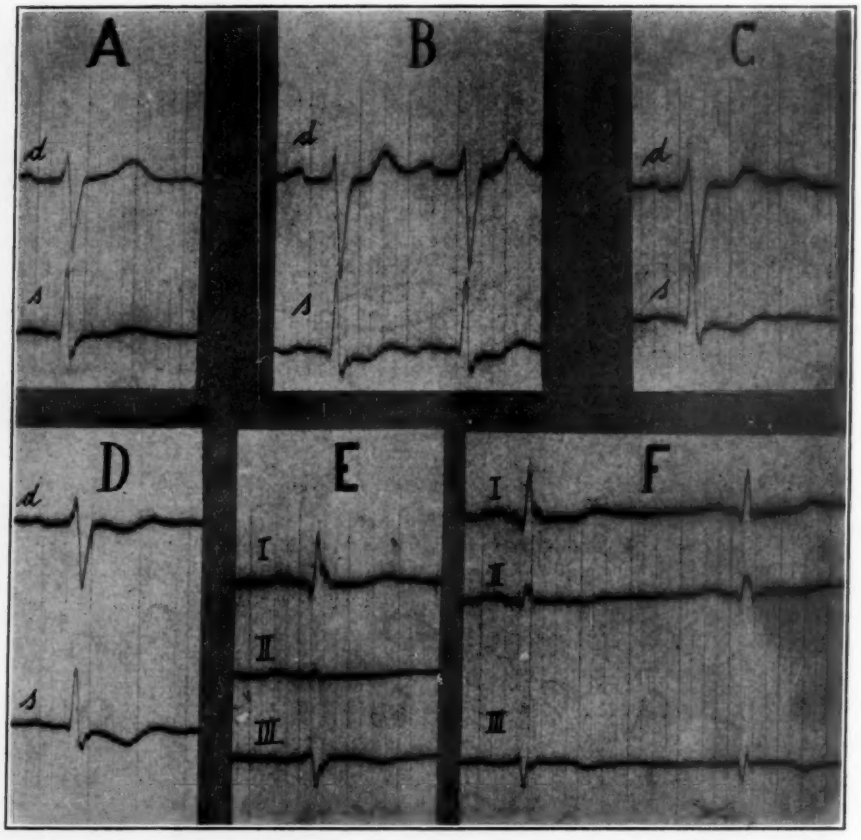

Fig. 6.—J. P. N. Working electracardiogram: *A*, thoracic lead before work; *B*, 30 seconds after cessation of work; *C*, 1 minute after cessation of work; *D*, 2¾ minutes after cessation of work; *E*, extremity lead before work; *F*, extremity lead 2 minutes after work. (Time marker, 0.05 second; 1 millivolt—20 mm.)

Ergometer Test (Fig. 7).—The maximal output of work was 500 kg-m per minute. The working capacity was limited by precordial pain. All three tests show a negative pulse curve shortly after the cessation of work.

Working Electrocardiogram (Fig. 8).—Ergometer tests on three different days show uniform electrocardiographic changes. Cessation of

work is followed immediately by a marked depression of the S-T interval in both thoracic leads. Both intervals take an almost horizontal course and turn into T-waves which are still distinctly positive immediately after the cessation of work; then the T-waves become diphasic

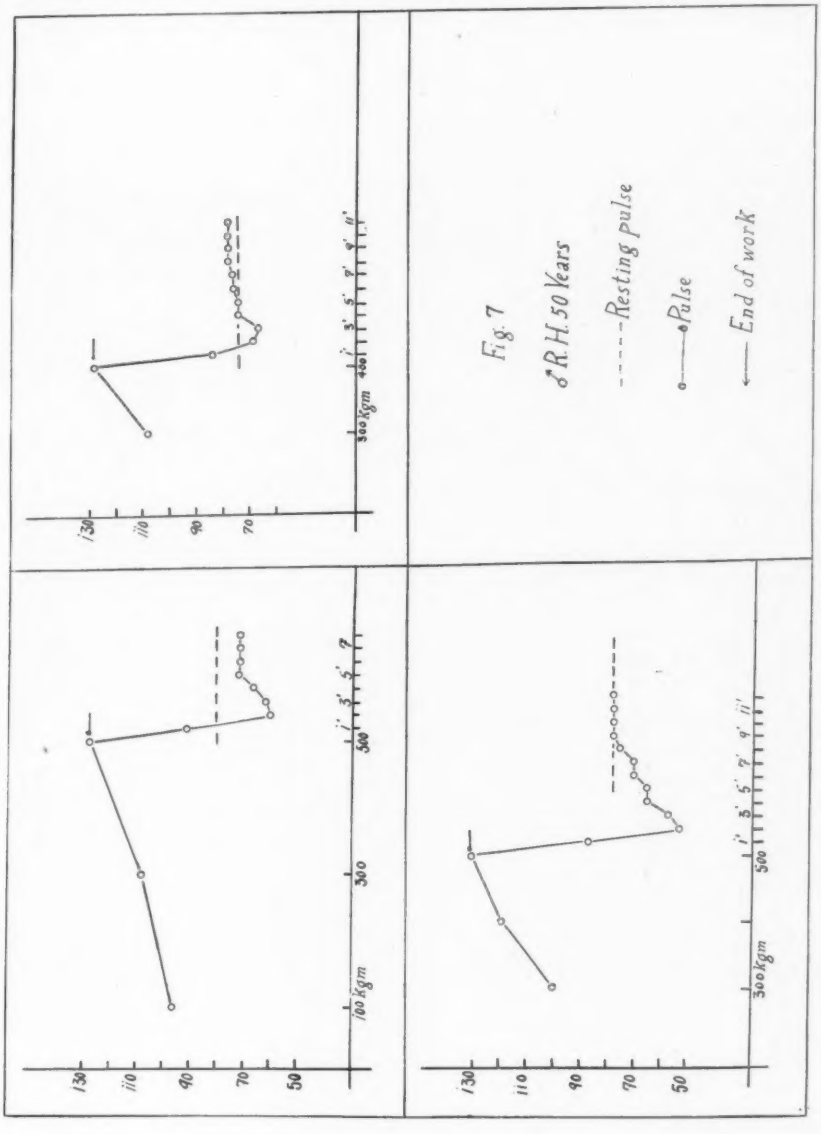

Fig. 7.—Ergometer tests on April 12, 13, and 15.

with a steadily increasing negative part and a steadily decreasing positive part. About two minutes after the cessation of work the S-T intervals are considerably less depressed, and now they are followed by great, entirely negative T-waves. These changes soon begin to regress, however, and the T-waves become entirely positive once more, after go-

ing through the diphasic stage. But it took nine minutes after the cessation of work before the electrocardiogram had the same appearance as prior to the work. In this case then the electrocardiogram in nine minutes goes through the same phases it otherwise takes some weeks or months to go through, after an acute attack of coronary thrombosis. On comparison with records *E* and *F* (Fig. 8) the corresponding changes

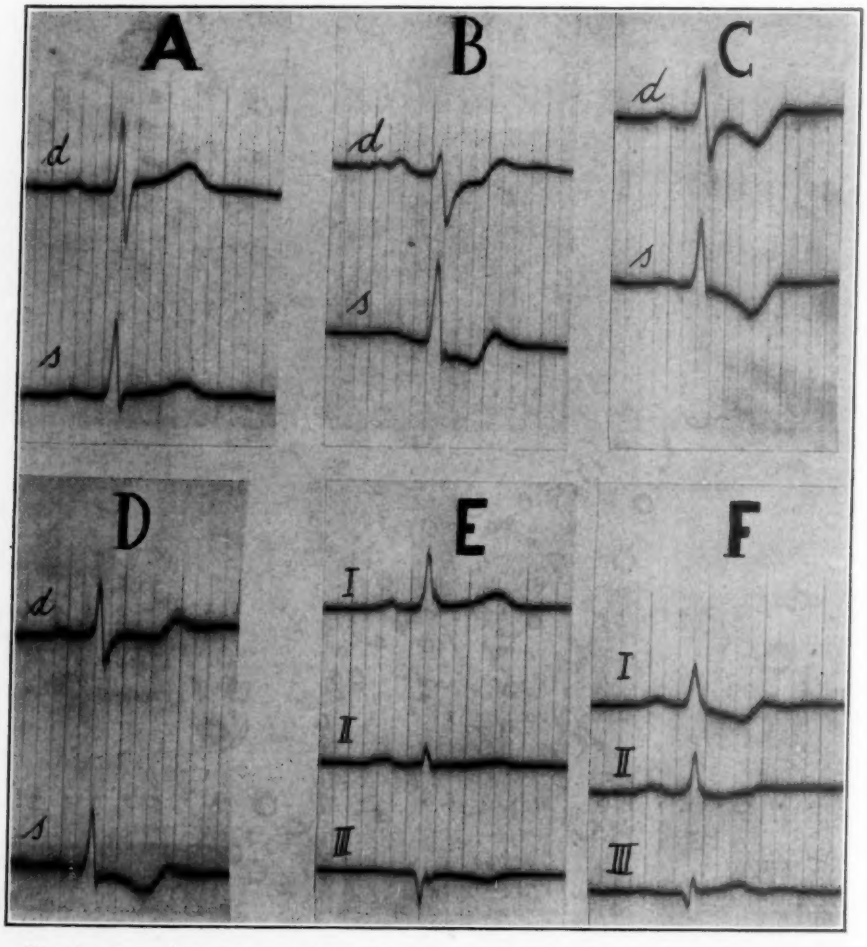

Fig. 8.—R. H. Working electrocardiogram: *A*, thoracic lead before work; *B*, 15 seconds after cessation of work; *C*, 2 minutes after work; *D*, 5 minutes after work; *E*, extremity lead before work; *F*, extremity lead 1½ minutes after work. (Time marker, 0.05 second; 1 millivolt—20 mm.)

in extremity leads are seen to be: Depression of S-T_1 and S-T_2 and elevation of S-T_3. T_1 is positive before the work; after work it is negative, or diphasic with a preponderance of the negative part. T_2 remains unchanged, low positive; T_3 changes from negative to positive. These changes also regress in about nine minutes after cessation of work.

CASE 4.—H. G., male, fifty-three years old, had scarlet fever in childhood; otherwise he gave a past history of good health. During the last half year before admission to hospital the patient had been troubled a little, while working, with dyspnea without palpitation of the heart or edema. During the month preceding examination he had had a sensation of precordial oppression, and rapid walking had

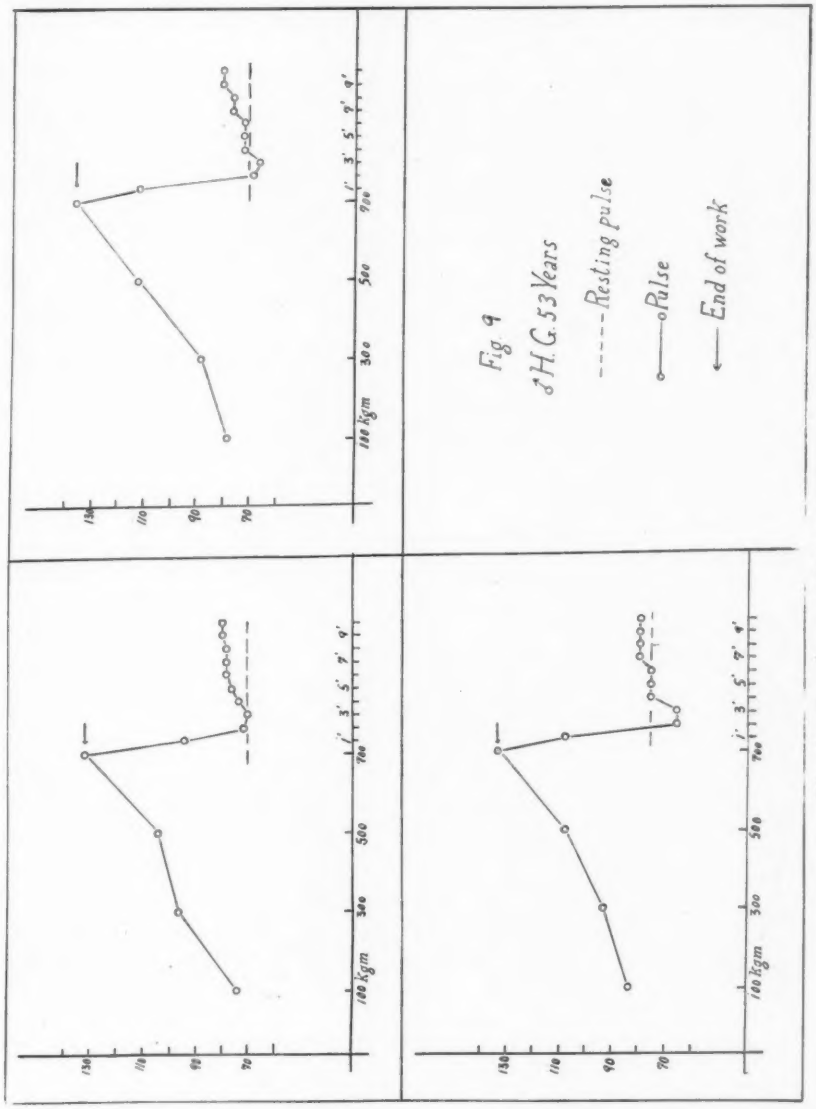

Fig. 9.—Ergometer tests on June 8, 11, and 12.

been followed by pain on the lateral surface of both arms. Once the pain appeared in the night. There was no pain in connection with meals or changes in temperature. The patient was a heavy smoker.

Physical Examination.—Nutrition was fair. There was no dyspnea or cyanosis at rest. Auscultation: The heart was partly lung-covered; the impulse of the apex beat was made out indistinctly in the fifth intercostal space, 1 cm. inside the

papillary line. The sounds were faint but clear; $A_2 > P_2$. No stasis was demonstrable in the lungs, liver, or legs. No myopathic processes were demonstrable in the muscles of the chest.

Special Examinations.—Wassermann and Kahn tests were negative. Sedimentation test (one hour), 2 mm.; blood pressure, 130/80; hemoglobin content, 112 per cent. The urine showed no abnormalities. Roentgenography of the heart: Dilatation of the left ventricle (demonstrable in the second oblique diameter); diffuse

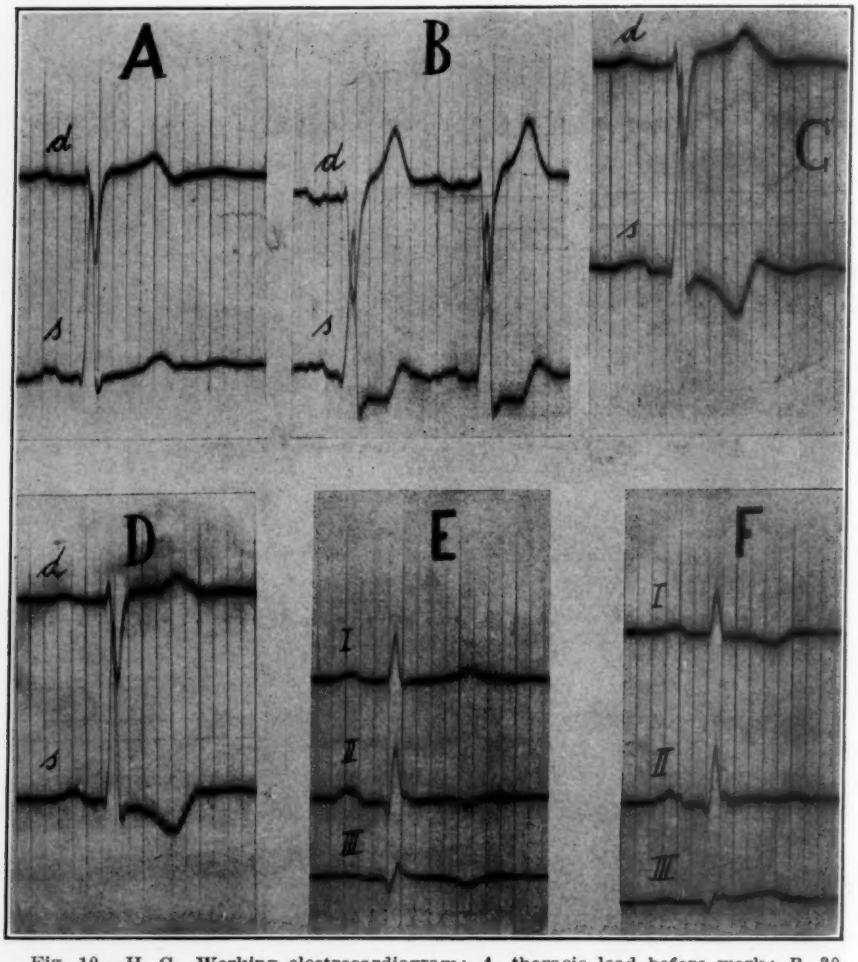

Fig. 10.—H. G. Working electrocardiogram: *A*, thoracic lead before work; *B*, 30 seconds after work; *C*, 4½ minutes after work; *D*, 6 minutes after work; *E*, extremity lead before work; *F*, extremity lead 5 minutes after work. (Time marker, 0.05 second; 1 millivolt—20 mm.)

dilatation of the aorta (8.5 cm.). Roentgenography: lungs, no abnormalities; peripheral arteries, distinct arteriosclerosis. Registration of heart sounds: No abnormalities. Electrocardiography: Isoelectric or very low T_3.

Summary of Positive Findings.—Accentuation of A_2, roentgenologically demonstrable dilatation of the left ventricle and aorta, peripheral arteriosclerosis.

Diagnosis.—Dilatation of the aorta, hypertrophy of the left ventricle, arteriosclerosis, coronary sclerosis (?).

Ergometer Test and Working Electrocardiogram (Figs. 9 and 10).—The records show similar changes, of about the same duration, as in the preceding cases.

DISCUSSION

These four patients, then, are men about fifty years old who complain of more or less typical anginoid pain during work. Two of these cases (Cases 2 and 4) represent probably a fully established condition of coronary sclerosis; in the other two cases the evidence of some organic heart lesion (in particular, coronary sclerosis) is more uncertain. At any rate, one would hesitate very much to designate these two patients as disabled (the Danish Act of Invalidity Insurance requires a decrease of the working capacity to less than one-third in order to designate an applicant as disabled). In these cases the ergometer test proves to be a valuable supplementary examination, as the above mentioned working tests can hardly leave any doubt about these patients' being quite unfit for manual work.

As mentioned, we have never encountered the negative pulse curve in normal persons, and we have seen it only in a certain number of cardiac patients. As far as our experience goes, the occurrence of this type of pulse curve is decidedly of pathological significance, but nothing definite is known about the cause of this peculiar phenomenon. With a view to the accompanying electrocardiographic changes, the idea suggests itself that this phenomenon involves a relative anoxemia of the myocardium, but this idea is contradicted by the fact that anoxemia experiments as a rule give an increase of the pulse rate even in the presence of pronounced electrocardiographic changes. If, nevertheless, one would maintain the possibility of this idea, one would have to imagine at any rate that the myocardial anoxemia which is produced during work is more pronounced than the myocardial anoxemia resulting from inspiration of oxygen-deficient air. There is another possibility: namely, that it may be a question of a central phenomenon. One might imagine, for example, that bradycardia of central origin produces an inadequate coronary circulation and, with this, the electrocardiographic changes. This theory is contradicted by the fact that the patients present no other cerebral symptoms; moreover, in one of the cases here reported (Case 3) an anoxemia test gave cerebral anoxemia with convulsions, loss of consciousness, and a slow pulse without electrocardiographic changes. Finally, we cannot refute the possibility that the bradycardia and the electrocardiographic changes may be two independent phenomena, coinciding merely by chance so that, for instance, the bradycardia may be due to sclerosis of the cerebral arteries, while the electrocardiographic changes result from sclerosis of the coronary arteries. In that case, however, one would expect on examination of arteriosclerotic patients now and then to find the negative pulse curve as an isolated phenomenon

without electrocardiographic changes, but we have never so far observed such a phenomenon in our working tests. For the sake of completeness, it is to be mentioned that blood sugar determinations have shown that the peculiar course of this pulse curve is not due to a decrease in the blood sugar concentration.

In our ordinary functional tests for estimation of working men's disability and similar conditions we have been accustomed to look upon the rapid pulse after work as a criterion of heart disease. To us it seems interesting, therefore, to learn that there are cardiac affections that manifest themselves only by a slow pulse after work.

SUMMARY

A report is made of four patients with clinical evidences of heart disease who, after work with Krogh's bicycle ergometer, presented the unusual feature of a prompt drop in the pulse rate to a rate below the resting level and at the same time showed transient gross changes in the electrocardiogram.

REFERENCES

1. Larsen, Kaj: On Electrocardiographic Changes in Deficiency of Oxygen, Report of the Seventeenth Scandinavian Congress of Internal Medicine, Acta med. Scandinav., 1935.
2. Groedel, F. M.: Das Extremitäten-Thorax- und Partial-Elektrokardiogram des Menschen, Dresden and Leipzig, 1934, Theodor Steinkopff.

ACROCYANOSIS: A STUDY OF THE CIRCULATORY FAULT*

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AN INSTANCE of acrocyanosis was first adequately described by Cassirer[1] in 1900 under the name of "acrocyanosis asphyxia chronica." Nothnagel,[2] as early as 1866, mentioned a patient who, to judge from a rather inexact description, may have been a sufferer from this disorder. Although regarded as rare by the earlier authors, we find the condition mentioned frequently in present medical literature, and there can be little doubt that at least in mild form it is a widespread malady. With the development of modern methods for the study of peripheral circulatory phenomena, it is surprising that, with the exception of Lewis' and Landis' recent contribution,[3] which will be discussed later, little exact knowledge as to the vascular mechanism has been elucidated.

Our interest in acrocyanosis was aroused by its presence in a patient having bilateral cervical ribs.

CASE REPORT

A married white woman, twenty-nine years old, complained of having had cold, blue, moist hands since childhood. She had always lived in a temperate climate and had never suffered from frost-bite or chilblains. Otherwise the past history was irrelevant with the possible exception of bimonthly attacks of migraine for years. The blueness of the hands and the sweating of the palms were worse during the winter months, when the hands were immersed in cold water, or when she was emotionally disturbed. For five years she had noticed inconstant pain, numbness, and tingling in the region of the radial aspect of the left elbow.

She was a slightly built, alert individual with a low blood pressure and a rather rapid resting pulse rate. Physical examination was noninformative except for the appearance of the hands. The fingers were long and tapering, and the skin was soft and pliable. With the hands dependent, blueness of the skin, most pronounced over the dorsal surface of the knuckles, could be traced upward to where it stopped abruptly shortly above the level of the styloid process. The palmar surfaces were likewise cyanotic, especially in the creases. Swelling was never present. The radial and ulner pulses were equally vigorous, and they did not fade when the arms were elevated above the shoulders. No sensory changes of the forearms or hands were demonstrable.

A roentgen ray study of the neck disclosed bilateral, short, thick, cervical ribs. The left rib down to its vertebral attachment was surgically removed, with immediate relief of the unpleasant sensations about the left elbow.

The patient has been studied over the period of a year since this procedure.

The operation has been without effect on the circulatory disturbance of the hands, according to observations during this time. The behavior of the left hand in reference to the experimental procedures later to be described has been identical

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with that of the right. We believe it improbable that the cervical ribs have contributed toward the circulatory disturbance in this patient's hands because: (1) it is extremely unlikely that irritation of vasomotor nerves from rib pressure could have persisted unchanged since childhood without eventually causing degeneration of those fibers and resultant symptoms of vasomotor palsy; (2) removal of the rib left the malady uninfluenced; (3) as succeeding evidence will show, a local vascular defect exists which is not strictly dependent upon the innervation of the vessels involved.

In addition to this patient, a milder degree of acrocyanosis has been encountered in two healthy young men who have kindly lent themselves for study.

METHODS OF STUDY

Charts of skin color were prepared after the method of Thomas Lewis.[4] Three color scales of nine shades each were made and numbered as follows: scale 1, from the color of bloodless skin to that of skin engorged with arterial blood, *A, 1B, 1C, 1D, 1E, 1F, 1G, 1H,* and 1; scale 2, likewise from the cream color of bloodless skin to the color of skin engorged with purely venous blood, *A, 9B, 9C, 9D, 9E, 9F,*

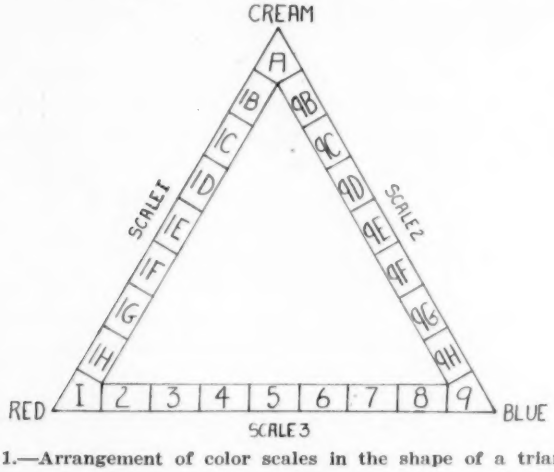

Fig. 1.—Arrangement of color scales in the shape of a triangle.

9G, 9H, and 9; scale 3 from the color of skin engorged with arterial blood through admixtures of increments of venous blood to the tint of blood in which all the hemoglobin has been reduced. Since these colors cannot accurately be reproduced, the scales may be arranged for the purpose of better visualization into an equilateral triangle as in Fig. 1. We have found these scales, although difficult to make, of great usefulness in confirming and recording objectively observations which otherwise are extremely liable to errors of subjective interpretation.

Measurements of peripheral pulse volume were made by the finger plethysmograph described by Scupham and Johnson.[5] Our instrument consists of a glass tube approximately the size of a finger. One end of the tube is closed by a rubber diaphragm with a hole in the center. From the other end, rubber tubing of small diameter is led off to the shaft of a 1.0 c.c. pipette containing a bubble of alcohol. The finger is inserted through the diaphragm into the glass tube, and the oscillations of the bubble, synchronous with the rise and fall of the finger volume with each pulse beat, are photographed on a moving film. To facilitate the comparison of data obtained by this instrument, we have devised a method of expression termed for convenience, "volume flow ratio." The distance between and the height of the waves are each measured directly in millimeters from the photographic tracings.

The former is divided into the latter, giving the ratio. If either the height of the wave increases (numerator) or the distance between the waves decreases (denominator), the ratio will increase, or in other words, will indicate an increment of total blood flow through the finger. Conversely, decrease in the ratio indicates lessening of the total blood flow. With the conditions remaining constant (i.e., length and bore of the tubing, distance of bubble from film, etc.), the changes in volume flow ratio may be compared under differing experimental conditions.

The greater part of this study was conducted in a room where temperature could be controlled to within 1° C. and relative humidity to within 10 per cent. Unless otherwise stated, skin temperature readings were taken from the pads of the fingers using a Leeds and Northrup galvanometer.

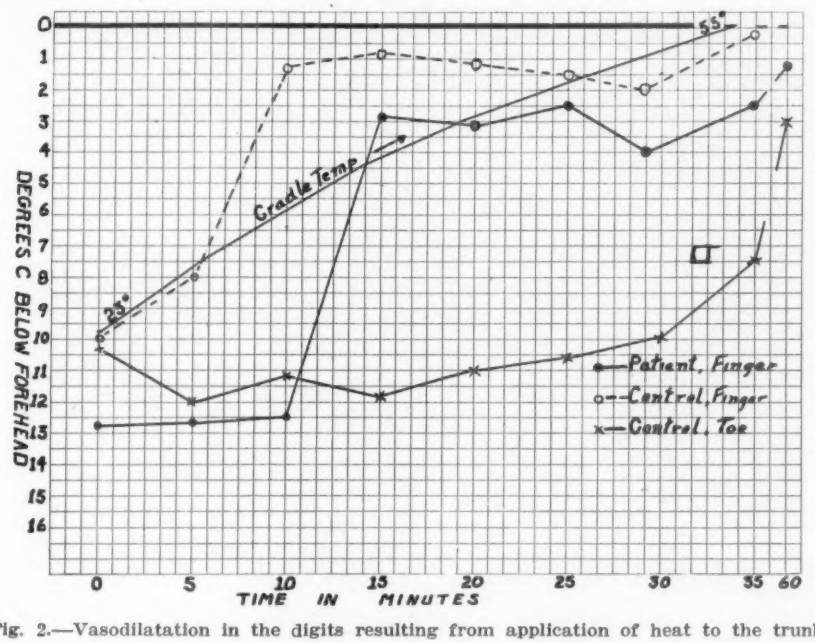

Fig. 2.—Vasodilatation in the digits resulting from application of heat to the trunk.

RESULTS

Response to Procedures Which Produce Maximum Vasodilatation.—After skin temperatures reached equilibrium with a room temperature of 24° C., the patient, clad only in a sheet, was placed in a wire cradle covered with blankets and heated by carbon filament lamps. The hands to the wrists and the head were exposed, and skin temperatures of the fingers and of a point above the bridge of the nose were read at five-minute intervals. Temperatures of the mouth and cabinet were likewise followed. Results are expressed graphically in Fig. 2. Temperature of the finger tips approximated that of the forehead in fifteen minutes, and capillary pulsation of the finger pads was noted at the twelfth minute. This response was checked by the method of Maddock and Coller,[6] in which the body is wrapped in blankets for one hour, and by immersion of two extremities in hot water during which the rise in skin tempera-

ture of the diseased limbs is followed, as described by Landis and Gibbon.[7] In all experiments the digital arteries widened quickly, equally, and fully as measured by the increase in skin temperature and in digital pulse volume. This response precludes the existence of structural arterial disease. The rapid and equal flushing of the fingers during reactive hyperemia after Lewis' method[8] was further evidence in this direction.

Response of the Hand Vessels to Varying Environmental Temperatures.—The spontaneous temperature and the color of this patient's fingers were observed almost daily during the summer and fall. The

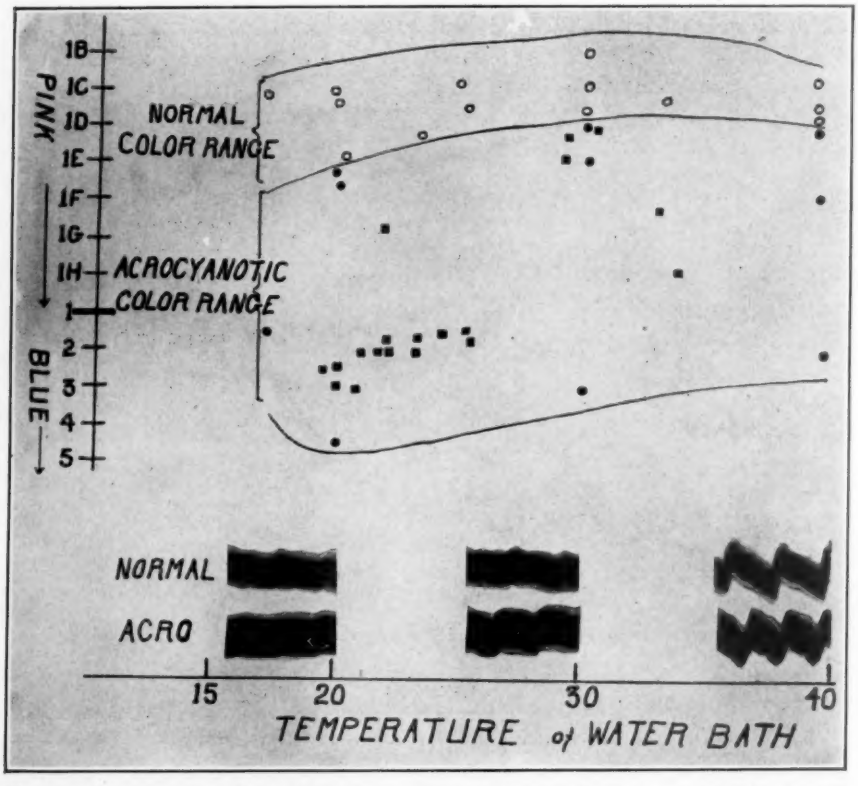

Fig. 3.—Color range and digital pulse volume of fingers at varying spontaneous and experimentally induced skin temperatures.

temperature of the room in which these observations were made varied from 15 to 30° C. during this period. An entirely normal color of the hands was never observed. At room temperatures below 24° C. there was uniformly a cyanotic tinge (color 2 to 4) and at higher temperatures cyanosis was often observed. If absent, it was replaced by an increase in pinkness not encountered in the skin of normal individuals in such an environment. Elevation of the hands above the head in the latter circumstances produced blanching to a normal depth of color. Temperature of the fingers was uniformly from 1 to 5° below that of the surround-

ing air. To test this matter under more carefully controlled conditions, the hands of this and of two other patients, together with those of normal individuals, were submerged in water baths at 15, 20, 30 and 40° C. for periods of ten minutes, and the effects upon the color of the skin and the digital pulse volume were studied. The range of observed color changes is given in Fig. 3. The circles represent colors after immersion in water and the squares, those occurring spontaneously at similar skin temperatures. A sample of the pulse tracings is also given. It will be observed that there is little overlap between the color range of normal and acrocyanotic hands under the conditions imposed. In the individuals tested we failed to confirm Lewis' statement[9] that the hands of normal

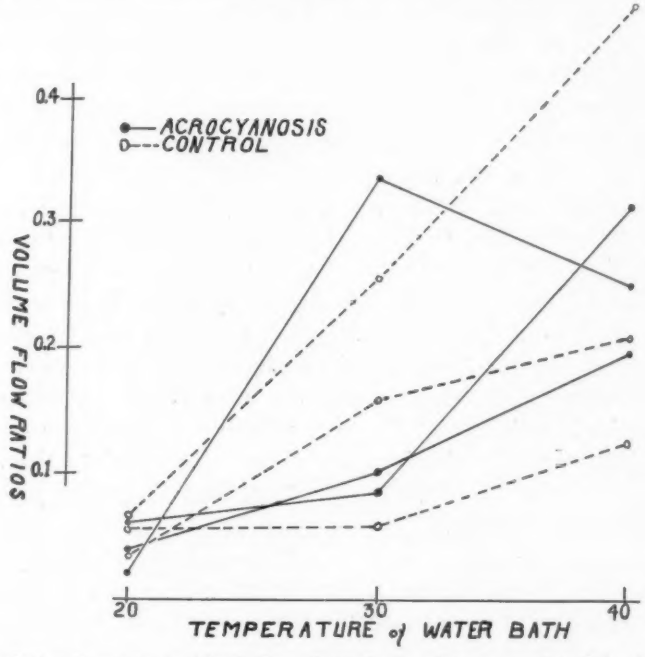

Fig. 4.—Relative increase in blood flow through the fingers produced by increase in external temperature.

persons may turn blue when subjected to a water temperature of 20° C., but this may be due to differences in room temperature, clothing, etc., prevailing in the two groups of experiments.

The changes in volume flow ratios of the fingers under these experimental conditions are charted in Fig. 4. Whereas possibly the ratios of the patients with acrocyanosis were slightly lower on the average than the normal after the immersion at 20° C., the normal increment in flow ratios with the subsequent increases in water-bath temperatures is evident. While the curves of increase of blood flow through the fingers are not as smooth as those published by Lewis and Landis,[3] this difference may be due to the method of measurement employed by us. We feel that these results are essentially in accord with those of these

writers. Their statement that the digital arteries in acrocyanosis respond in a normal manner to increments in local external temperature is justified.

An Evaluation of the Venous and Capillary Blood Flow.—The earlier writers, particularly Erben,[10] believed that in acrocyanosis there was an obstruction to the venous return because of increased tonus of the subcutaneous veins. He found that the subcutaneous venous network is poorly filled when the arm is experimentally congested, whereas the intracutaneous veins are overfilled and atonic. He postulated a "dissociation" in tonus between the intracutaneous and subcutaneous venous networks. Lewis has disproved the conception of venous obstruction by relatively simple observations which we have easily confirmed in the following manner: Our patient's hands, at a uniform temperature and tint of blueness (color *4*), were placed on a table at a level 8 inches below the heart. One hand was then elevated above the head for intervals of one, two, five, and ten seconds, respectively, after which it was quickly lowered to the table and the color immediately matched on the color scales. After one second's elevation, the hand was less blue (color *2*); after two seconds, pink (color *1F*); and after five and ten seconds' elevation a deeper pink was observed (color *1G* to *1H*). In other words, on elevation of the hands the blood quickly drained away from the capillaries and collecting venules. When the hand was lowered, these vessels rapidly refilled. Lewis and Landis[3] offer further evidence that there is no venous obstruction by observations of capillary pressure during and following closure of the arm veins by a pneumatic cuff. The capillary pressure, after having reached a point equal to the pressure imposed upon the veins, immediately returned to the precongestion level upon deflation of the cuff.

In this connection two other observations are worthy of note. 1. With the hands of our patient at heart level, light pressure upon the skin produced an area of blanching which did not return to its previous color until six seconds had elapsed, whereas a normal skin, subjected to the same procedure, returned to its former color after three seconds. The significance of this observation will be commented upon later. 2. With the patient's hands below heart level, an entirely normal depth of skin color was never observed, regardless of the temperature of the skin. If the fingers were pink, however, elevation of the hands above the head would, as previously mentioned, result in paling to a normal appearance. We believe that this phenomenon is due to the fact that at all times the minute vessels of this patient's skin are dilated. The depth of color therefore is a passive result of the amount of blood circulating in them, the degree of filling being dependent upon the arterial inflow and the venous drainage, factors obviously related to the position of the hands relative to the heart.

Many observers[11, 12, 13] have commented upon the dilatation of the capillaries, particularly of the venous side of the loop, as rather charac-

teristic of the microscopic appearance of the nail bed in acrocyanosis. This was strikingly evident in our patient regardless of the temperature and color of the skin at the time of observation. There is no need to recapitulate the details of the microscopic morphology as we cannot add to the descriptions of other workers.

The refractoriness of the minute skin vessels of the patient was further evidenced by a study of the response to adrenalin and nitroglycerin, as follows: After the patient, her trunk and legs covered by a woolen blanket, had been at bed rest for one hour in a room temperature of 18° C., the hands were blue (color *3*), and the temperature of the fingers had fallen to 16.8° C. Nitroglycerin $\frac{1}{100}$ grain was then placed under the tongue, and the blood pressure, pulse, finger temperature, color, and microscopic appearance of the capillaries were recorded at five-minute intervals. The blood pressure fell slightly in five minutes. The pulse quickened by 20 beats. The color and temperature of the fingers as well as the appearance of the capillaries did not alter over a period of thirty minutes. There was a slight increase in the digital pulse volume which lasted but a short time. Adrenalin, 0.75 c.c. of a 1:1,000 solution, was then injected intramuscularly and the observations were continued for thirty-five minutes more. The blood pressure changed from 110/70 to 128/55 after fifteen minutes, and the pulse increased from 90 to 118 per minute. Again the skin color and temperature remained unchanged. The capillaries became questionably less distinct.

Much emphasis cannot be placed upon the results of an uncontrolled experiment of this kind. We feel, however, that the apparent nonreactivity of the skin vessels, particularly as regards adrenalin, may indicate a loss of their tonus.

Response of the Minute Vessels to Histamine.—Lewis has emphasized the fact that if histamine is pricked into normal skin which has cooled spontaneously to about 20° C., little or no rise of temperature occurs in the region of the resultant flare. Pricked into acrocyanotic skin at a similar temperature, histamine produces a rise of several degrees. Since this is one of the primary evidences upon which Lewis bases his conception of spasm of the skin arterioles as the cause of acrocyanosis, we have attempted, unsuccessfully, to confirm his observations. Our determinations are listed in Table I. Using the utmost care to duplicate Lewis' technic, we found a susprising lack of consistency in behavior of the normal and acrocyanotic skin, both in the same individual on repeated tests and in different individuals. We are unable to explain these inconsistencies satisfactorily. It may be that the skin of the normal individuals tested varied so extremely in sensitiveness to histamine as to overshadow any constancy in response on the part of acrocyanotic skin. We can testify, however, to the vivid pinkness of the flare when histamine is introduced into acrocyanotic skin which is spontaneously cool or made cold by immersion in water. According to our observations,

the pinkness of the flare is exaggerated by the surrounding blue tint but does not exceed, either in depth or tint, that present in normal skin under similar circumstances.

Studies to Differentiate Between the Effects of Centrally Mediated Vasomotor Tone and Local Response of the Vessels to Cold.—We have found it difficult to evaluate the importance of vasomotor impulses of central origin in producing the symptoms presented by our patients. One young man stated that his hands turned blue if his body became chilled from any cause or if he became emotionally disturbed. We verified these statements on several occasions. Mrs. H., in whom we may safely assume that the cervical ribs played little rôle in increasing vasomotor tonus, gave a similar history. We have frequently seen her hands extremely blue under conditions in which the external temperature and lightness of clothing could not be invoked as the explanation. On one occasion, in the space of one minute, her fingers turned from pink to

TABLE I

TEMPERATURE RESPONSE TO INTRACUTANEOUS HISTAMINE

NORMAL					ACROCYANOSIS				
SUBJECT	ROOM TEMP.	INITIAL FINGER TEMP.	FINAL FINGER TEMP.	DEGREES RISE	SUBJECT	ROOM TEMP.	INITIAL FINGER TEMP.	FINAL FINGER TEMP.	DEGREES RISE
E. M.	18.2	18.8	19.6	0.8	S. H.	18.2	15.6	16.4	0.8
R. E.	18.2	18.8	19.0	0.2	S. H.	18.2	18.0	16.2	1.8
R. E.	14.4	18.8	20.0	1.2	D. R.	14.4	18.4	19.4	1.0
A. E.	18.2	19.2	25.0	5.8	S. H.	18.2	18.6	19.6	1.0
D. O.	17.8	19.4	19.7	0.3	S. H.	18.2	20.5	26.6	6.1
R. E.	23.8	21.0	27.0	6.0	S. H.	24.4	22.0	24.6	2.6
A. E.	18.2	22.6	30.4	7.8	D. R.	21.6	25.0	30.6	5.6

blue as the result of apprehension over an imminent hypodermic injection. The question is, therefore, whether these patients have a heightened vasomotor tone, or a normally responsive vasomotor apparatus which at times serves to accentuate a local vascular fault. This question is difficult to answer. Lewis has described the behavior of the acrocyanotic finger deprived of its vasomotor nerve supply by local-anesthetization of the ulnar nerve. We have studied the response to this procedure on four occasions in three patients. In each instance parallel observations were conducted upon a normal person. The results of a typical protocol are expressed graphically in Fig. 5. The liberty has been taken of adjusting the length of duration of anesthesia in the normal individual so that his temperature curve more nearly coincides, for purposes of comparison, with that of the acrocyanotic patient. The temperatures of the right second and fifth fingers of the former and of the right third and fifth fingers of the latter are expressed on the chart in terms of degrees below forehead temperature as better expressing the vasomotor gradient than would the actual readings. Before anesthesia the temperature of the patient's fingers was 12.5° C. below that of the forehead, whereas that of the normal fingers was only about 4° C. cooler. Within

ten minutes after anesthesia became manifest in the acrocyanotic hand, the temperature of the blocked finger had risen 8°. Color changes were carefully watched during this period because Lewis had found that the temperature of his patient's finger rose some 5° before pinkness appeared. He regarded this as indicating that, whereas the digital arteries opened quickly, the skin arterioles, initially in spasm, did not dilate primarily as a result of the nerve palsy but rather through the relaxing influence of the increased stream of warm blood coming to them from the larger vessels. This he accepts as additional evidence of arteriolar spasm in acrocyanosis. We can confirm this observation, as the color of our patient's fifth finger showed no sign of pinkness until the temperature had risen 7°. At this point the finger and ulnar side

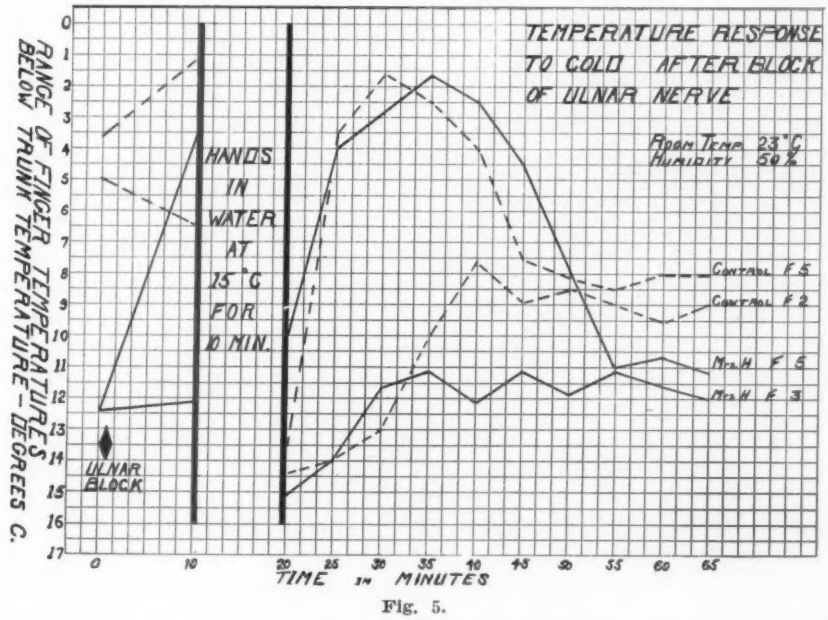
TEMPERATURE RESPONSE TO COLD AFTER BLOCK OF ULNAR NERVE
ROOM TEMP. 23°C HUMIDITY 50%
HANDS IN WATER AT 15°C FOR 10 MIN.
ULNAR BLOCK
CONTROL F 5
CONTROL F 2
MRS. H F 5
MRS. H F 3
RANGE OF FINGER TEMPERATURES BELOW TRUNK TEMPERATURE—DEGREES C.
TIME IN MINUTES

Fig. 5.

of the hand became vivid pink over a sharply demarcated area slightly exceeding the limits of anesthesia to pin prick. However, according to our observations there may be no appreciable change in color of the anesthetized normal finger even though its temperature exceed by 10° that of its neighbors. Therefore we cannot accept Lewis' deduction from this evidence without reservation.

When the temperature of our patient's anesthetized finger had reached a maximum, the hand was immersed in water at 15° C. for ten minutes and the color carefully observed. Whereas this finger retained a great share of its original color, the tint soon partook of a slight but definite blueness. Although its temperature was nearly at the preanesthetic level when read immediately upon withdrawal from the water, it rose 11.5° C. within five minutes—an effect parallel to that of a normal anesthetic

finger. By comparison, the temperature of the patient's third finger did not rise above the preanesthetic level.

These observations indicate that the major vessels of the acrocyanotic finger, when deprived of their vasomotor innervation, behave normally in response to local cold but that the minute skin vessels continue to exhibit a defective reaction.

In an attempt to study further the relative importance of centrally mediated or reflex vasomotor tone as against the purely local vascular reaction, the following experiment was devised: A patient with acrocyanosis was placed in a bathtub with water at a temperature of 21° C. and reaching to midchest, while the hands were immersed in a water bath for periods of ten minutes respectively at the following temperatures: 17 or 21°, 30°, and 40°. At the conclusion of each immersion period the color of the knuckles and finger nails together with the temperature of the fingers were immediately charted. After these readings the temperature of the bath water was increased to 30 and 40°, and the above observations were repeated. A similar experiment was conducted upon a normal individual. Results are given in Table II. Cyanosis of the finger nails was observed in the acrocyanotic patient at all immersion temperatures of bath water and hand bath, until the temperature of the former reached 40°, at which time plunging the hands into water at 17° failed to produce blueness. With the body bathed in water at 21 and 30°, however, immersion of the hands in water at 40° abolished the cyanosis of the fingers, the nails remaining blue. The highest skin temperature at which cyanosis of the finger nails persisted

TABLE II

SKIN COLOR RESPONSE TO VARYING ENVIRONMENTAL BODY AND HAND TEMPERATURES

TEMP. OF BATHTUB (° C.)	TEMP. OF HAND BATH (° C.)	COLOR OF HANDS	COLOR OF FINGER NAILS	SKIN TEMP. OF FINGERS (° C.)
		Acrocyanosis		
21	21	2	9*E*	23.0
21	30	2	9*E*	25.0
25	40	1*E*	9*C*	29.0
30	17	2	9*D*	21.0
30	30	2	9*E*	26.0
30	40	1*F*	9*D*	29.0
40	17	1*G*	1*G*	22.0
40	30	1*E*	1*E*	30.0
40	40	1*G*	2*H*	33.0
		Normal		
21	21	1*E*	1*E*	22.0
21	30	1*D*	1*D*	25.8
21	40	1*D*	1*D*	33.0
30	17	1*G*	1*G*	20.0
30	30	1*D*	1*D*	28.8
30	40	1*F*	1*F*	35.0
40	17	1*G*	1*G*	21.8
40	30	1*F*	1*F*	31.0
40	40	1*H*	1*H*	33.2

was 29°, and cyanosis of the hand, 26°. No cyanosis of the nails or hands of the normal individual was induced by any combination of bath-tub or hand bath temperatures, and the observed finger temperatures did not vary greatly from those of the patient.

The interpretation of these findings is perhaps as follows: With the patient's body bathed in water at a temperature below the average of the skin of his trunk, vasoconstrictor tone is reflexly heightened and accentuates the local vessel fault of the hands to the extent that cyanosis is not dissipated, even by the dilating influence of a hot hand bath. Conversely, when the body is bathed in water warmer than the skin, vasoconstrictor tone is apparently lessened to the extent that cyanosis can no longer be induced by cold. There is another possible explanation: that heat applied to the body, besides lessening or abolishing vasoconstrictor tone, stimulates vasodilator fibers which, as Lewis[14] has shown, may reach the vessels of the arm. The fact that the acrocyanotic finger, deprived of its vasomotor nerve supply, may turn blue when immersed in cold water, whereas no blueness is observed in a hand bath of similar temperature when the body is warmed, is further evidence in this direction. In the first instance vasodilator fibers, as well as vasoconstrictors, are paralyzed; in the second, vasodilator fibers are intact and probably stimulated reflexly by warmth applied to the trunk. The validity of this conception would be strengthened by a study of the behavior of the anesthetized acrocyanotic finger under experimental conditions similar to those above. If such a finger became blue in cold water, even though the body were warmed, the phenomenon described would be due not to warmed blood reaching the hand, but rather to the intervention of vasodilator impulses. Unfortunately we have been unable to perform this experiment.

DISCUSSION

What is the exact nature of the vascular fault producing acrocyanosis?

In the first place, the theory based on obstruction to the venous drainage from the hand, either functional or structural in nature, has been disproved. As Lewis and Landis[3] point out, Erben's observation that the subcutaneous veins are poorly filled was misinterpreted, as the smallness of the veins accompanied, rather than caused, coldness of the hands. The major arterial trunks of the hands, including the digital arteries, are likewise neither structurally nor functionally deranged sufficiently to explain the syndrome. The search therefore narrows to a consideration of the arterioles and minute vessels of the skin including the capillaries, collecting venules, and subpapillary venous network. Lewis and Landis regard an abnormal reactivity of the skin arterioles to cold as the cause of acrocyanosis. This conception is based fundamently upon two lines of positive evidence. They cannulated the venous end of a capillary loop in the nail bed and, after obstructing the venous return by a pneumatic cuff about the arm, determined the length of time needed

for the capillary pressure to equal that imposed upon the veins by the cuff. Normally this adjustment required three to four minutes, but in their acrocyanotic patient the time was as long as eight minutes. This, they argued, indicated that the flow of blood into the capillaries was retarded by the arterioles. We are in doubt as to the interpretation of this observation. It seems possible that if the vascular bed just beyond the arterioles be widely dilated, the pressure of the inflowing arteriolar stream, even though normal, might be dissipated in a vascular area of greatly increased cross-section. Hence the rise in capillary pressure would be delayed until this area becomes engorged.

Their second line of positive evidence is the differing response to histamine of the acrocyanotic and normal skin at a similarly cool temperature. As already stated, they observed in the former a rise of several degrees in temperature in the region of the flare, while in the latter little or no rise was encountered. From this they argue that when the skin of an acrocyanotic hand and a normal hand are both at a spontaneously cool temperature, the former is so primarily because the skin arterioles are in spasm, whereas the coolness of the normal skin is traceable to constriction of the digital arteries. In the one instance, relaxation of the skin arterioles by histamine produces a rise in temperature indicative of increased arteriolar blood flow; in the other, the larger arteries are not relaxed by histamine, and hence increase in arteriolar blood flow is negligible. We were unable to verify these observations and so are not convinced of the validity of Lewis' hypothesis.

Our interpretation of the available evidence leads to the conclusion that the primary vascular fault in acrocyanosis is a dilatation and refractoriness to stimuli of the capillaries and venules of the skin. The state of engorgement of these minute vessels is a passive result of the amount of the blood brought to and leaving them. The evidence may be briefly summarized. There is direct morphological demonstration that these vessels are dilated. The distribution of this disorder over the most dependent portions of the extremities, where the minute vessels are subjected to hydrostatic pressure in the veins, with its tendency to cause engorgement of even a normal hand, is well explained on this basis. The hands of our patient never exhibited an entirely normal appearance except when elevated above her head, a position which obviously favors drainage of blood from the minute vessels. With the hands dependent, pressure upon the skin left a pale area which was slow to fill. This might be due to slowed arteriolar inflow but more probably indicates a larger cross-section of empty vessels to be filled than is present in a normal skin under similar circumstances. As regards the nonreactivity of the capillaries to stimuli, we could not determine that in our patient there was any change in their caliber in response to cold, heat, adrenalin, or nitroglycerin. These observations, however, should be repeated and extended.

We do not wish to imply that there is no abnormality of reaction on the part of the arterioles in acrocyanosis, but only that in our opinion this is not the primary fault. Slowing of the arteriolar blood flow through any cause, be it a reaction to cold, to heightened vasomotor tonus, or to drugs, would materially exaggerate this fault, particularly if at the same time the minute vessels are subjected to the effects of hydrostatic pressure through the veins. That increased irritability of the vasomotor system may play a rôle in the production of this syndrome can hardly be affirmed or denied from the available evidence.

We should like to add that acrocyanosis should not be regarded necessarily as evidence of disease elsewhere in the body, as is somewhat commonly assumed.

SUMMARY

1. Experimental studies dealing with the nature of the circulatory mechanism which produces acrocyanosis are reported.

2. The evidence indicates that the primary vascular fault lies in dilatation and lack of response to stimuli of the minute skin vessels. The clinical picture depends upon the passive filling of these vessels as influenced by the amount and nature of the blood in them.

3. The rôle played by the tonus of the sympathetic nervous system, as opposed to the local reaction of the vessels to thermal stimuli, is discussed. Observations dealing with the effects of certain vasoactive drugs upon the vascular fault are presented.

REFERENCES

1. Cassirer, R.: Die vasomotor-trophischen Neurosen (Monograph), Berlin, 1912, S. Karger, pp. 506-535.
2. Nothnagel: Zur Lehre von den vasomotorischen Neurosen, Arch. f. klin. Med. **11**: 173, 1866.
3. Lewis, T., and Landis, E. M.: Observations Upon the Vascular Mechanism in Acrocyanosis, Heart **15**: 229, 1929-31.
4. Lewis, T.: Standard Colours for Use in the Study of Vascular Reactions of the Human Skin, Heart **15**: 1, 1929-31.
5. Scupham, G. W., and Johnson, C. A.: Peripheral Vascular Phenomena: The Peripheral Pulse Volume in Occlusive Arterial Diseases, Arch. Int. Med. **52**: 877, 1933.
6. Maddock, W. G., and Coller, F. A.: The Rôle of the Extremities in the Dissipation of Heat, Am. J. Physiol. **106**: 589, 1933.
7. Landis, E. M., and Gibbon, J. H.: A Simple Method of Producing Vasodilatation in the Lower Extremities, Arch. Int. Med. **52**: 785, 1933.
8. Lewis, T.: The Blood Vessels of the Human Skin and Their Responses, London, 1927, Shaw & Sons, p. 153.
9. Idem: Ibid. p. 145.
10. Erben, S.: Ueber vasomotorische Störungen, Wien. klin. Wchnschr. **31**: 33, 1918.
11. Vallaret, M., Justin-Besancon, L., Cachera, R., and Boucomont, R.: Les Acrocyanoses, Arch. d. mal. du coeur **27**: 725, 1934.
12. Parrisius, W.: Kapillarstudien bei Vasoneurosen, Deutsche Ztschr. f. Nervenh. **72**: 310, 1921.
13. Boas, E. P.: The Capillaries of the Extremities in Acrocyanosis: Blood Pressure and Morphology, J. A. M. A. **79**: 1404, 1922.
14. Lewis, T.: Vasodilatation in the Limbs in Response to Warming the Body: With Evidence for Sympathetic Vasodilator Nerves in Man, Heart **16**: 33, 1933.

DOUBLE AORTIC ARCH WITH TOTAL PERSISTENCE OF THE RIGHT AND ISTHMUS STENOSIS OF THE LEFT ARCH: A NEW CLINICAL AND X-RAY PICTURE

Report of Six Cases in Adults*

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THE diagnosis of congenital anomalies of the heart and large vessels is still a difficult problem, and it is only in exceptional cases that we are able to make a correct diagnosis in vivo and to confirm it by post-mortem examination. The fact that we have so few cases with careful clinical, roentgenological, and pathological findings makes it almost impossible at present to state definite clinical or roentgenological signs for a given anomaly. The six cases of double aortic arch (two confirmed by post-mortem examination) which I wish to report illustrate the great value of the x-ray in the diagnosis of such malformations. The opportunity of studying the first case clinically, roentgenologically, and at autopsy enabled the writer to recognize five more cases, and to establish a new clinical and x-ray picture by which the diagnosis of persistent right and left aortic arch can be made. This type is a form in which the right aortic arch takes its course over the right bronchus, then behind the trachea and esophagus. The left arch also persists, but with stenosis or atresia in the isthmus region.

The first case of this anomaly ever recognized during life was seen and diagnosed by the writer at the First Medical Clinic of the University of Vienna on Aug. 25, 1925. The diagnosis was confirmed at autopsy. The findings were presented before the Vienna Roentgen Society in October, 1925, and published in the *Wiener Archiv für innere Medizin* in 1926, along with two other cases observed clinically and diagnosed *intra vitam* but without autopsy. Since then the writer has added observations of three other cases with characteristic clinical signs and the same x-ray findings. The last case (Case 6 in this publication) was confirmed in every detail at autopsy. This makes a total of six cases observed, of which two were confirmed post mortem. We shall therefore discuss the embryological development of the aorta and its anomalies before describing this type of persistence of the right and left aortic arch with partial obliteration of the latter. This anomaly is of great interest from the evolutionary standpoint since it represents a reversion to the reptilian type of double aortic arch. Its clinical significance will be discussed later.

Most of the cases described in the anatomical and pathological literature have been cases of right aortic arch in which the descending aorta

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begins its downward course on the right side. This is the more usual form and has been described roentgenologically by Assmann in three cases. A study of the malformations of the great vessels also reveals the existence of double aortic arch, eight cases of which Poirier collected in 1896. In these cases the right or posterior aortic arch is usually the larger, the left or anterior arch the smaller. The trachea and esophagus lie between the two arches. The six cases which we shall describe belong to that type of double arch in which the large right arch lies retroesophageally and the small anterior left arch has undergone stenosis in the isthmus region. A right aortic arch may also be pulled to the left behind the trachea and esophagus by the ductus arteriosus when the left fourth arch is incomplete. In such cases the left descending dorsal aortic root is short or absent so that the condition of double arch does not persist as such.

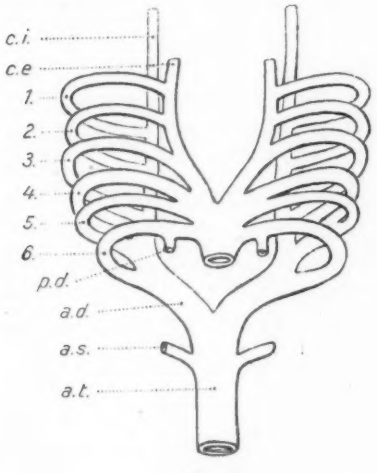

Fig. 1.

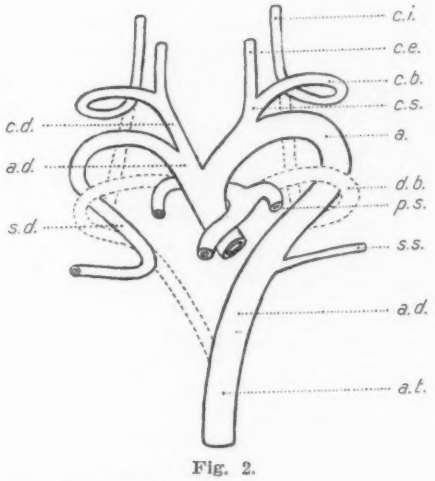

Fig. 2.

Fig. 1.—Diagram of the development of the large arteries:

c.i., internal carotid
c.e., external carotid
1 to *6*, aortic arches
p.d., right pulmonary
a.d., dorsal aortic root
a.s., subclavian artery
a.t., thoracic aorta.

Fig. 2.—Diagram of the development of the aorta and large arteries:

c.i., internal carotid
c.e., external carotid
c.b., carotid arch
c.s., left carotid
a., aorta
d.b., ductus Botalli
p.s., left pulmonary
s.s., left subclavian
a.d., dorsal aorta
a.t., thoracic aorta
c.d., right carotid
a.d., right innominate
s.d., right subclavian.

THE EMBRYOLOGICAL DEVELOPMENT OF ANOMALIES OF THE AORTA

For an understanding of the anomalies of the aorta we must first consider its normal development. In the third week of embryonic life we see the beginning of the development of the six aortic arches. The primitive aortic arch becomes the first branchial artery when the other five branchial arches develop between the primitive ascending aorta and

the primitive descending aorta. Thus the trunk goes over into six arches on each side. They do not all develop at the same time and are not all present at the same time. Some begin to disappear before others have appeared. The fifth soon recedes so that the sixth primitive arch later appears as the fifth, and the first and second also disappear. The remaining three are concerned in the development of the permanent vessels. The arches unite caudad to form two dorsal descending aortas, which fuse to form the common descending aorta (Fig. 1). From the sixth arch there grows on each side a main branch of the pulmonary artery. The portion of the right arch distal to the place of origin of the right branch disappears, while the corresponding portion of the left arch forms the ductus arteriosus Botalli. The left fourth arch forms the permanent aortic arch, the right the innominate artery and the beginning portion of the right subclavian artery. The dorsal communicating portion between the third and fourth arches disappears on both sides. The third arch forms the internal carotid, and the craniad persisting portion of the ascending aorta forms the external carotid. Finally the communication between the right fourth arch which forms the innominate artery and right subclavian and the permanent descending aorta disappears (Fig. 2).

With this brief discussion and a study of the two figures which illustrate the normal development, we shall have no difficulty in understanding the anomalies of the aorta and the large arteries. There are four chief types: (1) double aortic arch, (2) right-sided aortic arch, (3) absence of the aortic arch, and (4) origin of the right subclavian artery from the descending arch.

Double Aortic Arch

The ascending aorta may divide into two convex ascending aortas and arches which give off a subclavian, the external and the internal carotid, and then combine to form the descending aorta. Or, the ascending aorta may be normal and only the arch divided (Fig. 3). There is then an anterior and a posterior arch. The anterior or left arch originates from the left fourth branchial artery, and the posterior from the right. In these cases the trachea and esophagus usually lie between the two arches. We shall see that the anomaly of which we are describing six cases is closely related to this group. In double arch the anterior or left arch is usually smaller than the posterior or right arch.

Right-Sided Aortic Arch

This anomaly, which is the normal aortic type in birds, results from the persistence of the right fourth arch and right descending aortic root, while they in part or completely disappear on the left side (Fig. 4). The arch of the aorta goes over the right main bronchus and downward on the right side, as a rule; it may, however, go behind the trachea and esophagus, as in our six cases.

In most cases of right-sided aorta the arch and part of the descending aorta are located to the right of the vertebral column. With this abnormal position of the arch there are also abnormalities in the course of the left ductus Botalli because the right ductus almost always disappears. Although the aorta in these cases, as in birds, chooses the right

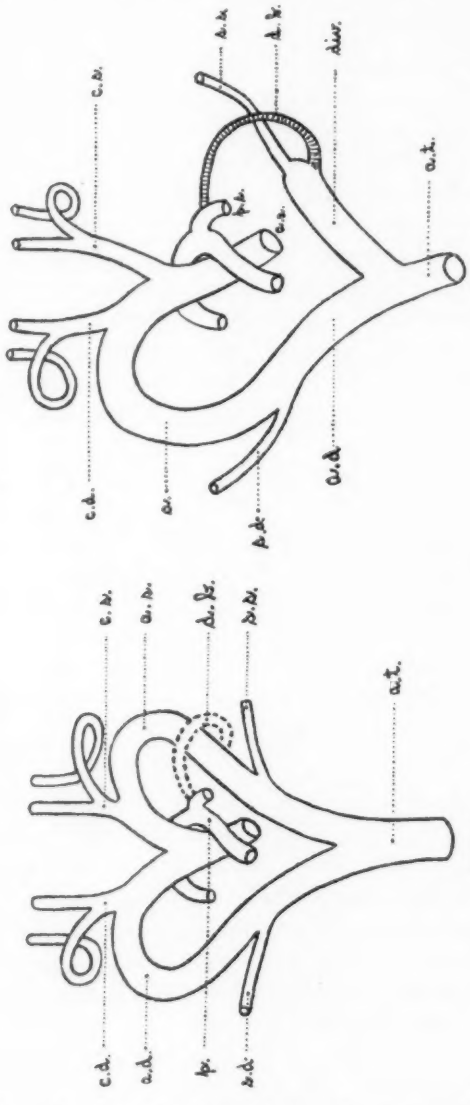

Fig. 3.

Fig. 3.—Diagram of the development of double aortic arch:

c.d., right carotid
a.d., right aortic arch (posterior arch)
p., pulmonary artery
s.d., right subclavian
c.s., left carotid
a.s., left aortic arch (anterior arch)
d.b., ductus Botalli
s.s., left subclavian
a.t., thoracic aorta.

Fig. 4.

Fig. 4.—Diagram of the development of the more common type of right-sided aorta (persistence of the right aortic arch) with right-sided arch:

c.d., right carotid
a., right-sided aorta
s.d., right subclavian
a.d., descending aorta
d.b., ductus Botalli
div., diverticulum (rest of left descending dorsal aortic root)
c.s., left carotid
p.s., left pulmonary
a.a., ascending aorta
s.s., left subclavian
a.t., thoracic aorta.

fourth arch and the right descending root, still the left ductus Botalli persists as in mammals. The result is that the ductus Botalli remains in close connection with the left descending aortic root and the left subclavian artery.

The left subclavian artery takes a very characteristic course in some of these cases. Holzapfel in 1899 collected twenty-one cases of abnormal

left subclavian artery in cases of right-sided aorta. In all, the left subclavian was the last branch of the right-sided aorta. In almost all the cases the beginning portion of the left subclavian (left descending dorsal aortic root) was enlarged. This diverticulum-like portion usually runs to the left behind the esophagus and gives off the left subclavian artery, and communicates with the left ductus Botalli (Fig. 4). The writer described such a case of right-sided aorta with retroesophageal left descending aortic root and left subclavian in 1926. The typical location for the left descending root is the place where the arch goes over into the descending aorta, usually at the level of from the second to the fourth thoracic vertebra. This constancy of location of the left subclavian is due to its close relation to the ductus Botalli. In cases of abnormal right subclavian artery this close relationship does not exist, and hence the origin of abnormal right subclavians is quite variable. If retrogressive changes occur in the left dorsal aortic root then the abnormal left subclavian may originate from the left ductus Botalli. In 1922 Goldbloom also collected examples of anomalous right subclavian artery.

Absence of the Aortic Arch

The arch of the aorta may be entirely absent, or only the isthmus (portion lying between the origin of the subclavian artery and the insertion of the ductus Botalli) closed or entirely absent. There is then no communication between the ascending and the descending aorta. When the fourth arch and the lateral communicating branch between the fourth and sixth arch become obliterated, then the sixth arch and left descending aortic root may remain open. The ascending aorta then supplies the vessels of the head and the right subclavian, and the open ductus Botalli goes over into the descending aorta on the left side.

TOTAL PERSISTENCE OF THE RIGHT AORTIC ARCH AND ISTHMUS STENOSIS OF THE LEFT AORTIC ARCH

The six cases which we shall describe represent an intermediate type between persistence of both aortic arches and persistence of the right aortic arch. We have in our cases the persistence of both aortic arches, total of the right which has the size of a normal aorta, and partial occlusion of the left arch which may be looked upon as an isthmus stenosis. We shall see that it is the persistence of the left aortic arch (in the form of the left subclavian artery, a short occluded vessel, and the left descending dorsal aortic root) which is responsible for the location of the arch behind the trachea and esophagus in our cases. The writer was able to demonstrate in the roentgenograms of the patients not only the right-sided retroesophageal aorta but also the shadow of the left dorsal aortic root which looks like a diverticulum and lies behind the esophagus. We have therefore named this anomaly "right-sided retro-

esophageal aorta," or "total persistence of the right and partial stenosis of the left aortic arch." This is in contrast to a type of right-sided aorta described by Assmann.

The three cases of so-called high right-sided aorta (*hohe Rechtslage der Aorta*) described by Assmann represent the type of right-sided aorta with right-sided arch which we have already discussed (Fig. 4). The name used by Assmann is unsatisfactory because it does not explain the nature of the anomaly and can easily be confused with right-sided displacement of a normal aorta by pathological conditions in the chest, such as fibroid pulmonary processes, exudates, pneumothorax, tumors, etc. I therefore suggested in 1926 the term "right-sided aorta," or persistence of the right aortic arch instead of "high right position of the aorta." In the cases described by Assmann, the aorta runs over the right bronchus and the arch remains on the right side. We have already seen that this anomaly represents most of the cases of right-sided aorta described by anatomists and pathologists. The x-ray picture is that of an aortic knob on the right side in the right sternoclavicular region. The aortic band usually seen in the right oblique position is visible in the left oblique as a pulsating curved shadow over the right bronchus. In the right oblique position the aortic band is lighted away by the trachea and left bronchus except for a small narrow strip just above the heart. The x-ray examination of the esophagus is not mentioned in the three cases. From the above discussion of this anomaly we can see that this is very important because in this form of right-sided aorta with right-sided arch the left descending dorsal aortic root or the left subclavian artery or ductus Botalli is found behind the esophagus.

Because anomalies of the heart, as well as of the aorta, were found in Assmann's cases he assumed that right-sided aorta or persistence of the right aortic arch is associated with cardiac defects. Two of his cases had a subaortic ventricular septum defect with the aorta riding the defect. Assmann looked upon these as representing a definite type in which the aorta is usually wider and the pulmonary artery narrower than normal. The third patient possessed an abnormally narrow aorta which passed upward from the left ventricle over the right bronchus. There was also a large auricular septum defect. Dietlen, who described no cases of his own, states in his book on x-ray diagnosis of the heart that right-sided aorta occurs only in connection with other defects. Mohr also concludes that a *hohe Rechtslage* indicates the existence of ventricular septum defect. Sprong and Cutler point out that associated anomalies were common in their series of thirteen cases of right aortic arch with left innominate artery but no *situs inversus viscerum*. We shall see from our cases that persistence of the right aortic arch can occur without any malformations whatever in the heart. In our six cases there was no evidence in any of functional or organic cardiac disturbance; the hearts were all normal in size and form. The patients were all adults

and in all of the cases the anomaly was an incidental finding during a routine physical and fluoroscopic examination of the chest. In other words it produced no subjective symptoms. The two necropsied cases revealed a normal heart free from any anomalies. A persistence of the right aortic arch instead of the left is itself no cause for the existence of cardiac anomalies and bears no necessary relation to the embryologic development of the heart. We have seen ten hearts with persistence of the right aortic arch in various pathological museums and at autopsies and in nine of the ten the heart was entirely normal. A study of the literature reveals many anatomical specimens of right aortic arch with normal heart.

We shall see that there is a marked difference between the x-ray findings in right-sided aortic arch of the Assmann type and those in right-sided retroesophageal aortic arch first diagnosed by me.

This type of right-sided retroesophageal aorta belongs to the group of cases recorded in the older literature under the title "dysphagia lusoria," a term which should be dropped because of its inaccuracy. This phrase was used by Bayford in 1789 to describe a case of dysphagia which he considered to be due to the pressure of an anomalous right subclavian artery on the esophagus. Relatively few of such anomalies cause a dysphagia. In only one of our six cases in which the aorta is located behind the esophagus and displaces it forward and to the left was there any disturbance of swallowing. This one patient had a carcinoma of the cardia of the stomach. Had an aneurysm of the arch developed there would undoubtedly have been a dysphagia. Perhaps the term "arteria lusoria, with or without dysphagia" would be better for these cases.

CASES OF RIGHT-SIDED RETROESOPHAGEAL AORTA
(TOTAL PERSISTENCE OF THE RIGHT AORTIC ARCH AND PERSISTENCE WITH PARTIAL STENOSIS OF THE LEFT AORTIC ARCH)

CASE 1.—The patient, H. H., a man fifty years old, entered the First Medical Clinic of the University of Vienna on Aug. 19, 1925. His illness dated from June of the same year when he developed an acute angina with a fever of 39°C., lasting ten days. After an interval of four days he had a second attack lasting five days. Two weeks later the third attack brought him to the hospital. He had painful swelling of both ankles. The pains in the legs were so severe that walking was impossible. After a careful physical examination, which revealed no cause for his fever, the patient was sent to the x-ray laboratory for an examination of the chest. Here the writer saw him on Aug. 22, 1925.

The fluoroscopic examination revealed a darkening of both apices with a few small dense spots in the right infraclavicular area. There were some calcified glands in both hilums. The examination of the heart revealed an unusual picture such as the writer had not previously seen. Attention was immediately attracted to the presence of a dense shadow which ran upward from the right heart border just to the right of the sternum to the region of the head of the right clavicle, and to the

absence of the normal aortic knob to the left of the sternum. A careful examination with a small diaphragm showed the shadow to the right of the sternum to be sharply outlined and to run upward to the level of the right clavicle where it described a curve to the left and was lost in the shadow of the spine. This shadow showed a very distinct pulsation synchronous with the ventricular systole. On the left side there was found only a faint suggestion of an aortic knob instead of the normal prominent knob produced by the descending portion of the aortic arch.

The next thing that attracted attention was the fact that the trachea was displaced to the left, instead of to the right as is found normally (Fig. 5). The heart

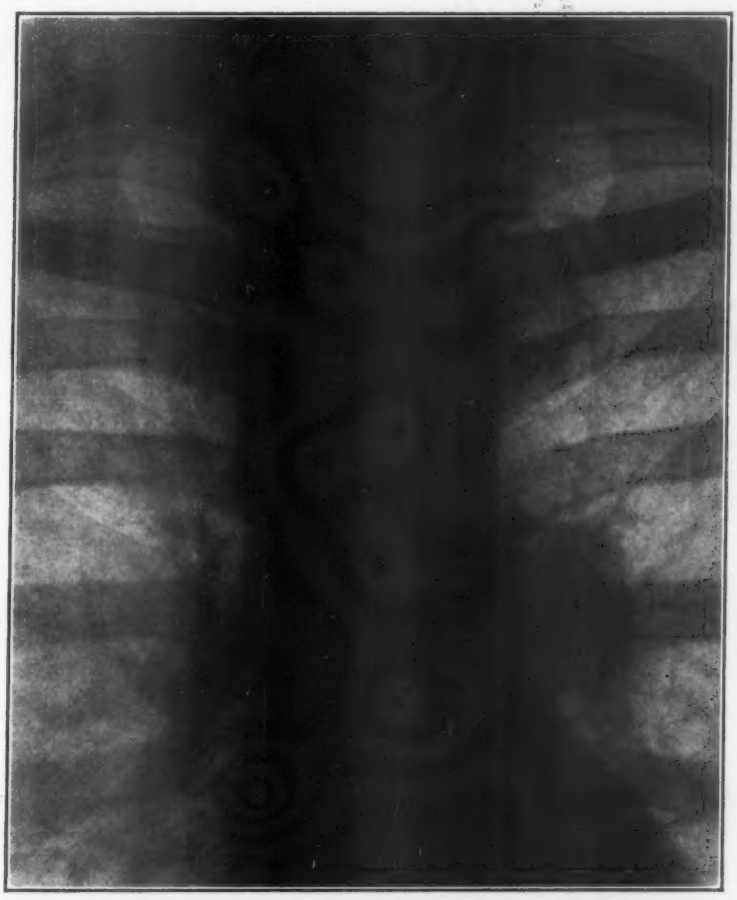

Fig. 5.—Right-sided retroesophageal aorta (persistence of the right aortic arch). The aorta runs upward on the right side, above the right bronchus, then behind the trachea and esophagus (Case 1, total persistence of the right, isthmus stenosis of the left aortic arch).

itself appeared normal except for a slight enlargement of the left ventricle. In the first (right anterior) oblique position a very interesting and new picture presented itself. The trachea, instead of running downward parallel with the spine, described a semicircular curve forward at the level of the upper border of the clavicles. It reached its maximum distance from the spine at a point behind the middle of the manubrium (Fig. 6). Just below this level the trachea divided into its two main branches. An examination of the esophagus with a barium paste showed a similar

circular displacement forward and to the left of the esophagus at the same level. A distinct pulsation could be seen against the posterior wall.

There was no aortic knob visible in front of the trachea in the first oblique position. There was found, however, a round shadow about 1¼ inches in diameter directly behind the displaced trachea and esophagus. This shadow showed a distinct

Fig. 6.—Total persistence of the right aortic arch, isthmus stenosis of the left aortic arch. The same patient as in Fig. 5, showing right anterior oblique view. The aortic knob is seen behind the trachea, which is displaced forward. In this retrotracheal knob can be seen the round shadow of the rest of the left descending dorsal aortic root.

systolic pulsation. The shadow was separated from the heart below by the trachea and right main bronchus. In the retroesophageal and retrotracheal shadow just described there can be seen a smaller, round, more intense shadow about ¾ inch in diameter.

In the second (left anterior) oblique position we saw the ascending aorta producing a wide pulsating shadow to the right of the trachea. It described a convex border and extended upward to the region of the upper border of the left clavicle, then ran downward to form the descending aorta which was visible in this position in front of the spine.

The diagnosis made on August 25 after an examination of the photographs was: so-called high, right-sided position of the ascending aorta, which is distinctly visible above the right heart border and to the right of the sternum, and runs over the right bronchus instead of the left. In the first oblique position the ascending aorta

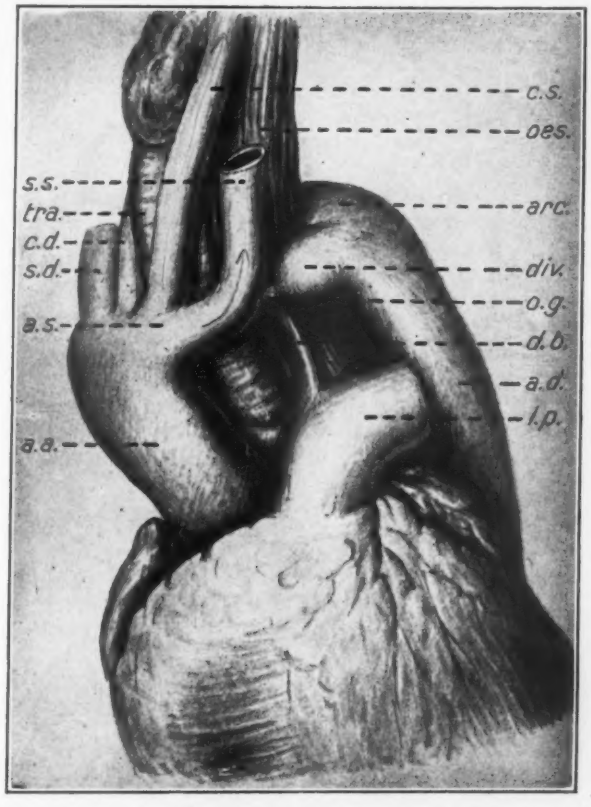

Fig. 7.—Drawing of heart and aorta from Case 1, viewed from the left side. Here we see the right-sided aorta running over the right bronchus, then behind the trachea and esophagus. The ring around the trachea and esophagus formed by the right-sided aorta and the left aortic arch (left subclavian artery, occluded short vessel, and diverticulum) is distinctly visible.

c.s., left carotid
oes., esophagus
arc., arch of aorta
div., diverticulum
o.g., occluded vessel
d.b., ductus Botalli
a.s., left innominate
a.d., descending aorta
l.p., left pulmonary
s.s., left subclavian
tra., trachea
c.d., right carotid
s.d., right subclavian
a.a., ascending aorta.

is partly lighted away by the trachea and right bronchus. No aortic knob is visible in front of the trachea. A round pulsating shadow lies behind the trachea and esophagus and displaces these forward and to the left. This shadow most likely represents the aortic arch behind the trachea and esophagus.

Blood and spinal fluid Wassermann tests were negative, also tests for typhoid and paratyphoid bacilli. The patient died on Sept. 17, 1925. The autopsy was per-

formed by Dr. Feller at the Pathological Institute of Prof. Maresch. Death was due to a generalized periarteritis nodosa. We shall describe only the heart and great vessels which are of interest here.

There was hypertrophy of the left ventricle. Otherwise, the auricles and ventricles were entirely normal. There was no congenital anomaly of the heart; the auricular and ventricular septa were normal; and the foramen ovale was closed. All of the valves were normal. An examination of the aorta revealed a right-sided aorta which ran upward over the right bronchus and then horizontally and downward behind the trachea and esophagus. The trachea and esophagus were displaced forward and to the left. There was a deep impression in the posterior wall of the esophagus which formed the bed for the aortic arch. At the beginning of the descending aorta and behind the left posterior border of the esophagus there was a diverticulum, or pouch, which projected from the anterior surface of the aorta. The diverticulum also made a depression in the left margin of the esophagus to which it was attached by loose connective tissue. The pouch was 1.8 cm. in diameter and 1.5 cm. in length. From this diverticulum of the aorta two occluded vessels branched off, one to the left subclavian artery and the other to the left branch of the pulmonary artery. The former corresponded to the isthmus of the normal left-sided aorta and the latter represented the ductus Botalli. A short distance below the diverticulum the aorta ran downward and mediad, forming the thoracic aorta. The right-sided retroesophageal aorta was of normal size. The valves were normal. The first branch of the ascending aorta was a short left innominate artery which divided into the left subclavian and left carotid. The second branch was the right carotid, and the third branch the right subclavian. After giving off these three branches the aorta ran in the angle between the trachea and right bronchus and then curved to the left behind the trachea and esophagus. Where the arch went over into the descending aorta lay the diverticulum already described (Fig. 7).

We thus see that we are dealing in this case with a persistence of the right aortic arch which runs over the right bronchus and behind the trachea and esophagus. The shadow which was found behind the trachea and esophagus represents a retrotracheal and retroesophageal aortic knob. The trachea and esophagus are therefore displaced forward and slightly to the left. This picture is so characteristic that when it has once been seen it can be recognized immediately. The finding which is diagnostic of this anomaly is the characteristic displacement of the esophagus at the level of the arch, and this is clearly visible in the first oblique position. In fact, the dislocation of the trachea and esophagus to the left is even visible on posteroanterior fluoroscopic examination. We shall see later that there are other anomalous arteries which may displace the esophagus, but they usually occur below the level of the aortic arch.

The circular, more intense shadow seen on the photographs in the retroesophageal aortic knob in the first oblique position represents the diverticulum which we found on the anterior wall of the aorta where the arch goes over into the descending aorta. The size of the shadow, the sharp outline, and the location behind the trachea at the level of its bifurcation make this the correct interpretation of this shadow. The diverticulum is, as we shall see, the left descending dorsal aortic root to which the ductus Botalli and occluded isthmus are attached.

The characteristic x-ray findings in our case of right-sided retroesophageal aorta are therefore:

1. A sharply outlined shadow with systolic pulsation to the right of the sternum, which begins at the fourth right intercostal space, goes

Fig. 8.—Right-sided retroesophageal aorta (persistence of the right aortic arch) as seen in Case 2. Note the ascending aorta to the right of the esophagus, which is displaced to the left. There is no aortic knob on the left side. The pulmonary artery appears prominent.

upward in a very slight curve to the region of the right sternoclavicular joint, then in a convex curve to the left and downward producing a very small aortic knob to the left of the sternum. In younger individuals no knob may be visible on the left side.

2. In the first oblique position no aortic knob in front of the trachea, but instead a retrotracheal and retroesophageal aortic knob separated from the heart shadow by the trachea and right bronchus.

3. In this knob a circular darker shadow which represents the diverticulum or pouch (left descending dorsal aortic root). This shadow is not always demonstrable.

4. Dislocation of the trachea and esophagus forward in a semicircle and slightly to the left.

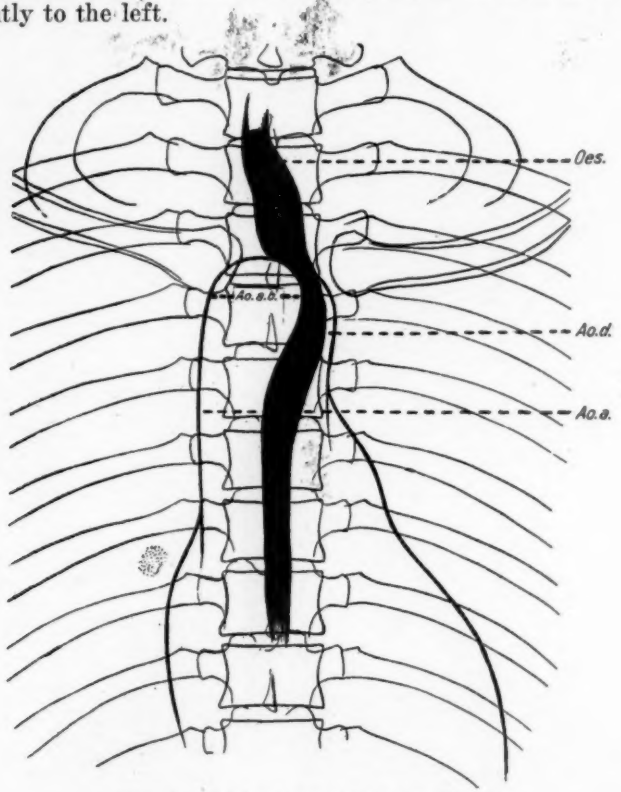

Fig. 9.—Explanatory sketch for Fig. 8:

Ao.a.b., width of ascending aorta
Oes., esophagus
Ao.d., descending aorta
Ao.a., ascending aorta.

5. Distinct systolic pulsation of the retrotracheal aortic knob shadow.

6. In the second oblique position a wide ascending aortic band visible to the right of the trachea and above the right bronchus.

CASE 2.—On Oct. 17, 1925, a young woman, aged twenty-five years, was sent to us for a fluoroscopic examination of the chest. This was required of her when she made application for a position as nurse in a children's hospital. She was a normally developed, healthy young woman with no cardiac or other complaints. On fluoroscopic examination the writer was at once impressed with the similarity between the findings and those just described in Case 1. The absence of the normal aortic knob on the left side, the characteristic shadow to the right of the sternum with its systolic pulsation and the slight displacement of the trachea to the left led us to think at once of the possibility of a right-sided retroesophageal aorta.

Having discovered the characteristic circular displacement of the esophagus at the level of the arch we at once gave the patient some barium paste to swallow and found the exact picture observed in our first case. The esophagus described a curve forward and to the left, then gradually returned to its normal position (Figs. 8, 9, 10, and 11).

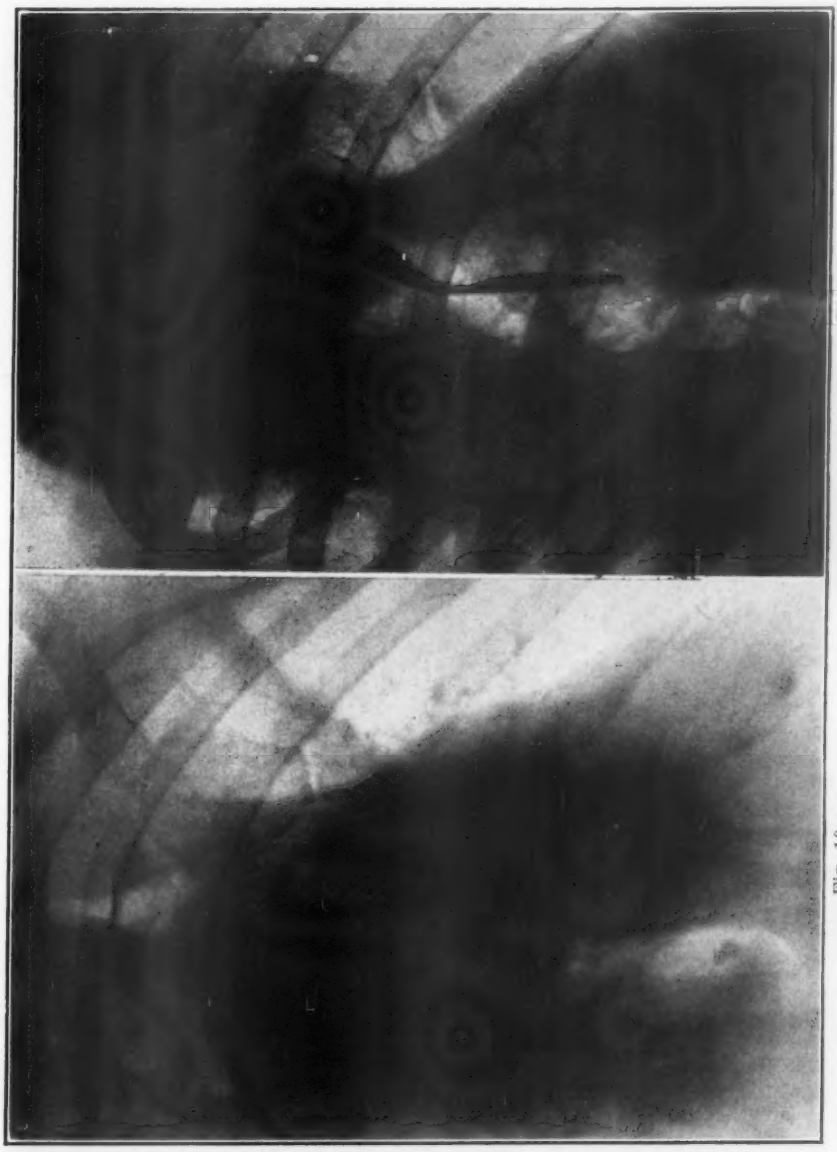

Fig. 11.

Fig. 10.

Fig. 10.—Right-sided retroesophageal aorta (Case 2) in the first oblique position. The trachea is displaced forward, and to the left, and the aortic arch lies behind the trachea. In the aortic knob a round shadow similar to that found in Case 1, is visible. This may be the diverticulum (left dorsal aortic root).

Fig. 11.—Right-sided retroesophageal aorta (Case 2) in the first oblique position, with the esophagus filled with barium. The esophagus is displaced forward in a curve at the level of the aortic arch, and reveals a distinct pulsation produced by the aorta against its posterior wall. This finding is characteristic of the anomaly.

We see from Figs. 8 and 9 that we have in these cases a method of determining the width of the ascending aorta by filling the esophagus with barium. With the normal aorta Kreuzfuchs has described this method for measuring the descending arch.

CASE 3.—On Feb. 4, 1926, the writer had the opportunity of seeing a third case of total persistence of the right aortic arch with the aorta behind the trachea and esophagus. The patient was a young man twenty-seven years old. He had a colloid goiter with marked enlargement of the thyroid gland and bilateral apical tuber-

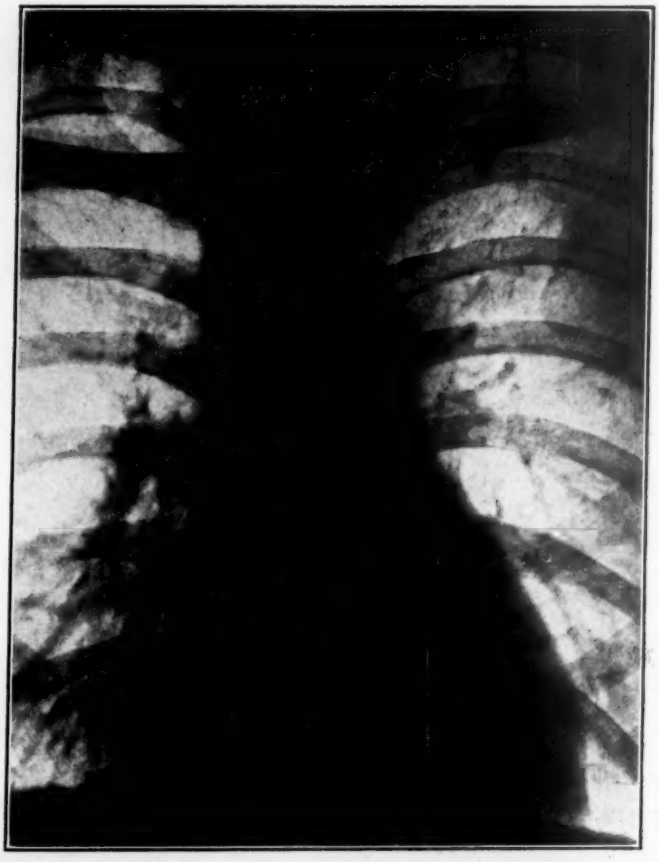

Fig. 12.—Case 3. Right-sided retroesophageal aorta. Note again the shadow of the ascending aorta which runs upward on the right side to the upper border of the clavicle. There is no aortic knob on the left side, and the pulmonary artery therefore appears prominent. The esophagus is displaced to the left by the descending arch. The heart is normal.

culosis. Again the x-ray findings were identical with those already described, except that the writer was not able to demonstrate to his satisfaction the round shadow of the diverticulum in the retroesophageal aortic knob. The other findings corresponded exactly with those which we have already detailed. The esophagus and trachea revealed the same diagnostic displacement. It is interesting that in the second and third cases in younger individuals the aortic knob was not at all visible on the left side. As a result, the pulmonary artery was more prominent than normally because it was not partly covered by the descending portion of the aortic arch (Fig. 12).

In this patient also the heart appeared normal, and the electrocardiogram was normal. There were no cardiac or other symptoms. There was no difficulty in swallowing.

In the second and also in the third case the writer found a clinical symptom which may aid one in suspecting the presence of right-sided aorta. In these two cases it was found on auscultation that the second aortic tone is heard best over the head of the right clavicle instead of in the usual place. The second pulmonary tone is found in normal position so that it is easy to differentiate the second aortic from the second pulmonary tone. The second aortic tone was louder than the second pulmonary tone in both cases. This finding is easily explained by the position of the right-sided aorta and its close proximity to the surface of the chest in the region of the head of the right clavicle. On percussion the right-sided aorta also produced a narrow band of dullness to the right of the sternum. In Cases 2 and 3 a pulsation was visible to the right of the sternum, in the second and third intercostal spaces.

CASE 4.—This patient, A. N., a forty-eight-year-old male, was examined on March 5, 1929. He was a stonecutter by occupation and had been engaged in this work for thirty-three years. The patient's chief complaint was marked shortness of breath which began in June, 1928. He continued to work until five weeks before examination. For the past six months the patient had had insomnia and orthopnea. There was dullness to the right of the sternum, with a visible pulsation in the second and third right interspaces. The aorta was palpable behind the head of the right clavicle. A definite tracheal tug was felt with the head elevated. The aortic second sound was heard best in the right supraclavicular fossa and in the first right intercostal space. Passage of a rigid stomach tube met with a resistance at the level of the third dorsal vertebra. At this point a distinct pulsation was transmitted along the tube to the finger tips. The tube could not be passed beyond this point since further pressure caused pain.

The fluoroscopic examination and photograph of the chest revealed normal apices. There was a marked increase in the lung markings around both hila due to passive congestion. In both lung fields there were numerous small irregular, sharply outlined spots. These were quite dense and were suggestive of a silicosis such as is seen in stonecutters. There was an obliteration of the right phrenicocostal angle by adhesions, with reduced mobility of the right diaphragm. The entire left phrenicocostal angle was occupied by a homogeneous dense shadow which extended upward over the apex of the heart. This shadow made it impossible to outline the apical region of the heart. The shadow was most likely due to thick pleural adhesions. (The patient had a severe attack of pneumonia with pleurisy nine years before, when he was sick for four months.)

The examination revealed an enlarged heart of aortic configuration. There was also enlargement of the heart to the right. Above the heart and to the right of the sternum was found the characteristic shadow of the ascending aorta. The shadow ran upward from the fourth intercostal space to the upper margin of the head of the right clavicle, where it curved to the left and again became visible behind the head of the left clavicle (Fig. 13). Here was seen, instead of a normal aortic knob, a small portion of the descending aorta running downward into the heart shadow. On account of a marked arteriosclerosis, the entire aorta was very distinctly visible. On posteroanterior fluoroscopy there was again the slight displacement of the trachea to the left at the level of the aortic arch. In fact, it was

this displacement of the trachea to the left which first attracted our attention. With barium paste we found the characteristic displacement of the esophagus in a curve to the left, visible on posteroanterior examination (Fig. 13).

In the first oblique position we found the identical picture of a retrotracheal and retroesophageal aortic knob such as we have already described in detail. The esophagus showed the anticipated semicircular forward displacement produced by the arch of the aorta (Figs. 14 and 15). We had again the characteristic picture of a persistence of the right aortic arch which takes its course behind the trachea and

Fig. 13.—Case 4. Showing the ascending aorta running upward on the right side above the level of the right clavicle. The esophagus is markedly displaced in a circle to the left. The descending aorta is just visible to the left of the esophagus. The heart is normal.

esophagus to reach the left side. The patient's clinical symptoms were due to cardiac decompensation, the result of marked silicosis, obliterative bilateral fibrous pleuritis, and emphysema. The aortic anomaly was an incidental finding as a result of the study of the previous three cases.

CASE 5.—This patient, Miss M. B., was seen by the writer on Nov. 23, 1931. She was then 24 years old. The patient had a severe cold, with symptoms of acute bronchitis which caused her to consult a physician. The patient had lived for one

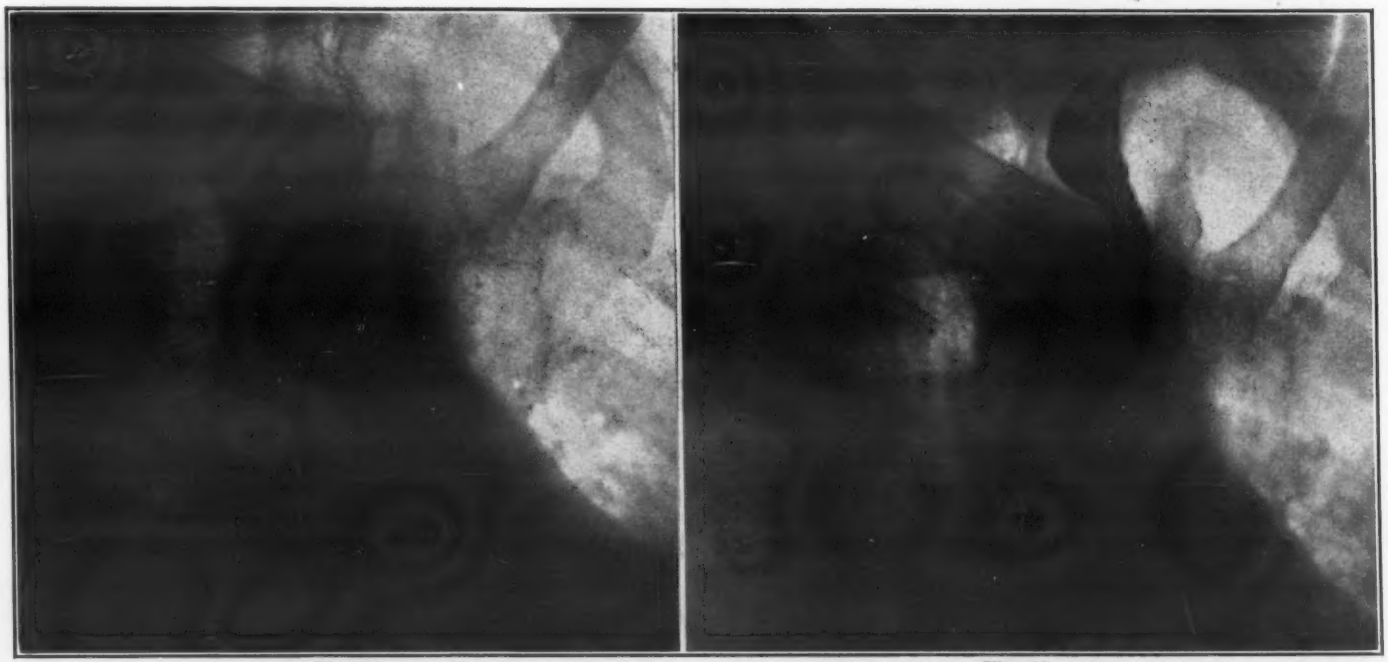

Fig. 14. Fig. 15.

Fig. 14.—Case 4. The first oblique position. The aortic arch lies behind the trachea, which is markedly displaced forward and to the left.

Fig. 15.—Case 4. The first oblique position, showing the esophagus filled with barium. Here the characteristic displacement is clearly demonstrated, with the aortic arch behind the esophagus and trachea.

week, in August, with a young woman who developed active pulmonary tuberculosis, and she feared infection. There was no history of pleuritis, or hemoptysis. The patient had always been well. There was no evidence of cardiac disease. The patient was normally developed. The Wassermann test was negative.

On physical examination I was attracted by finding a slight pulsation in the second and third right interspaces and a loud aortic second sound in the first right intercostal space, and even louder in the right supraclavicular fossa. There were no murmurs. A pulsation could be felt on deep pressure in the fossa. The trachea deviated slightly to the left. There was also a definite tracheal tug with the head extended. I suspected a right-sided retroesophageal aorta, and fluoroscoped the patient.

The findings were the same as those observed in the other four cases. The ascending aorta arose from the right heart border at the level of the third right interspace and extended upward 1 inch to the right of the right vertebral border. It described a convex curve to the right upward to a point 1 cm. above the upper border of the right clavicle. Here it made a sharp curve to the left with displacement of the trachea and esophagus to the left (Fig. 16). No aortic knob was visible on the left side, and the naked pulmonary curve formed the first convex curve of the left heart border. The heart was of normal size.

The oblique positions showed the characteristic displacement of the esophagus and the trachea, with the pulsating retroesophageal aortic arch. The electrocardiogram was normal.

Of interest were the clinical findings of a visible pulsation in the second and third right interspaces, a palpable aortic pulsation in the right supraclavicular fossa, maximum intensity of the aortic second sound in the right supraclavicular fossa, slight displacement of the trachea to the left, and a tracheal tug.

CASE 6.—This case is of interest because the diagnosis was made by the writer from the physical examination and was confirmed by x-ray examination and necropsy. We shall see that in this case the complete anatomical diagnosis of persistent right aortic arch behind the trachea and esophagus, with persistent left aortic arch in front of the trachea (consisting of the left subclavian artery, isthmus stenosis, and diverticulum or left descending dorsal aortic root), was made and was confirmed.

The patient, a white male, forty-six years old, entered the Cook County Hospital, Chicago, on the writer's service on April 6, 1932. The chief symptoms were vomiting immediately after swallowing solid food, weakness, loss of weight, and melena for about six months. The difficulty in swallowing followed upon the extraction of all his teeth. There was some epigastric discomfort but no pain.

The past history revealed a chancre at 18, with a four-plus Wassermann reaction on several recent examinations. He had a very severe attack of typhoid at the age of 20. A herniotomy had been performed five years before. He had had large varices of both legs for several years, with varicose ulcers of the left leg.

Of special interest to us at this time were the chest findings. We shall omit a description of the other conditions observed. There was a slight tracheal tug. The trachea was displaced about ½ inch to the left. There was a visible pulsation in the right first and second intercostal spaces. There was a visible and palpable pulsation in the right supraclavicular fossa, where a strong pulsation was easily felt on deep pressure. The aortic second sound was loud and ringing and heard best in the right first interspace and supraclavicular fossa. There was an area of dullness to the right of the sternum which extended upward to the right clavicle; it extended about 1 inch to the right of the sternum. There were no murmurs.

The heart was slightly enlarged to the left; the apex beat was in the fifth interspace in the midclavicular line. The transverse diameter was 5½ inches. The Wassermann reaction of the blood was four-plus. There was a secondary

anemia, and the feces were positive for blood. On passage of a stomach tube, an obstruction was met at the level of the third dorsal vertebra, and *a definite pulsation was transmitted along the rigid stomach tube.* The tube could be passed beyond this obstruction but met a second impassable obstruction at the cardiac orifice. (The patient had a carcinoma of the cardia of the stomach.)

The blood pressure was 196 systolic, 122 diastolic in the right arm, and 190 systolic, with 110 diastolic in the left arm. The electrocardiogram was normal.

The clinical diagnosis was: (1) double aortic arch, with persistent right arch over the right bronchus and behind the esophagus, and left arch with an isthmus

Fig. 16.—Case 5. A young woman twenty-four years old. The ascending aorta describes a convex curve to the right of the sternum, running upward above the right clavicle. The esophagus is displaced to the left, also the trachea. The descending arch is not visible. The heart is normal.

stenosis as described by the writer in Case 1 in August, 1925, and confirmed at autopsy. Furthermore, the other clinical findings not recorded in this paper added the following: (2) carcinoma of the cardia of stomach with liver metastases, (3) posttyphoid obliterative thrombophlebitis of both common iliac veins with collateral circulation, (4) syphilitic aortitis, (5) syphilitic endarteritis of cerebral arteries with areas of encephalomalacia.

The fluoroscopic examination of the chest presented a picture now very familiar to the writer, but one which could be easily overlooked.

The heart presented a normal appearance. Rising from the right heart border, at the level of the fourth right intercostal space, was a slightly convex shadow which extended upward to the right clavicle 1 inch to the right of the sternoclavicular joint. The shadow had a systolic pulsation synchronous with the heartbeat. The shadow formed a convex curve and ran across the vertebral column at the level of the third dorsal vertebra to reach the left side. It then ran downward from a point at the lower border of the head of the left clavicle in a convex curve to the left until it reached the left heart border in the third left intercostal space (Fig. 17). The trachea was displaced about ½ inch to the left of the median line. To the left of the trachea at the level of the fourth dorsal vertebra there was a more dense semicircular shadow in the shadow of the aortic arch.

The posteroanterior view (Fig. 17) differs from the pictures in the other five cases only in the more conspicuous shadow of the descending portion of the aortic arch and descending thoracic aorta. It will also be noted that the descending aortic border has a wavy outline. Second, a round, more dense shadow is easily seen to the left of the trachea in the beginning portion of the descending arch. The more prominent descending aorta with its slightly wavy outline was interpreted as due to a syphilitic aortitis, and the round, denser shadow was considered to be the diverticulum, or descending dorsal aortic root. The diagnosis of double aortic arch was made and proved by the oblique views and examination of the esophagus. Already in the posteroanterior view the characteristic displacement of the esophagus in a circular curve to the left at the level of the arch may be seen. In the present case the esophagus was displaced 1 inch to the left by the retroesophageal right aortic arch.

The first oblique position showed clearly the large retroesophageal aortic knob (right aortic arch) and a second much smaller knoblike shadow in front of the trachea. Between these two lay the esophagus and trachea (Fig. 18).

In the second oblique position the entire ascending aorta was visible to the right of the trachea, which is partly obscured 1 inch above its bifurcation by the arch where it lies behind the trachea. At this same level the esophagus and trachea describe a curve anteriad, due to the arch which runs around to the left side of both.

Here again we have conclusive proof of the presence of a persistent right aortic arch which runs over the right bronchus, then behind the trachea and esophagus. Furthermore, we have evidence of the existence of a diverticulum of the descending arch and of a left aortic arch as well.

The diagnosis which was made on April 20, 1932 was: total persistence of the right aortic arch with retroesophageal course, persistence of the left aortic arch in the form of a left subclavian artery, isthmus stenosis, and diverticulum or left descending dorsal aortic root; syphilitic aortitis, with widening of the aorta.

The patient died on June 17, 1932, from a severe hemorrhage of the stomach resulting from the carcinoma of the cardiac portion. The autopsy was performed by Dr. R. H. Jaffe, director of the Pathologic Institute. Only those findings which concern the heart and aorta will be given at this time.

The heart weighed 275 gm. The left ventricle was 18 mm., the right, 3 mm. thick. The myocardium was grayish brown and friable. *There were no anomalies in the heart.* The valves appeared normal.

The ascending aorta ran upward on the right side, in the direction of the head of the right clavicle. It made a slight convex curve to the right. It ran over the right main bronchus and behind the trachea and esophagus until it reached the left side. Its transverse diameter was 28 mm. Eight centimeters above the aortic valve it gave off its first large branch, the left innominate artery. This artery was 11 mm. in diameter and divided 20 mm. from its origin into the left carotid and the left subclavian artery. The left innominate and its bifurcation lay directly in

front of the trachea and 20 mm. above the bifurcation of the trachea. The left common carotid measured 7 mm. in diameter, the left subclavian 9 mm. (Figs. 19 and 20).

Forty millimeters from the origin of the left innominate and 20 mm. from the origin of the subclavian artery, the latter artery formed an angle of about 135

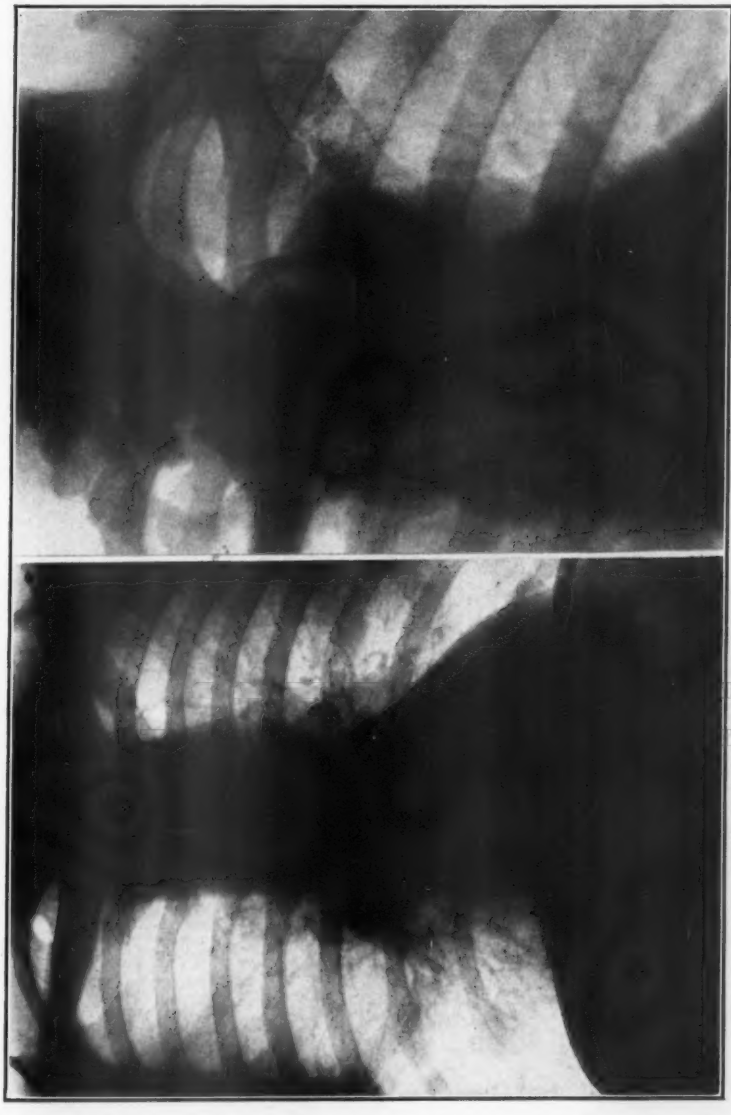

Fig. 17.

Fig. 18.

Fig. 17.—Case 6. Double aortic arch of the same type as the other five cases. This case is the second confirmed at autopsy by the writer. Here the ascending aorta is visible on the right side, and the descending aorta on the left side. The trachea is displaced to the left and compressed. In the descending arch, just below the head of the left clavicle, the shadow of the aortic diverticulum (left descending dorsal root) is distinctly visible. The heart is normal.

Fig. 18.—Case 6. The first oblique position. The esophagus contains barium. Note the wide syphilitic aortic arch behind the esophagus. There is a second smaller arch in front of the esophagus. The latter represents the left innominate and subclavian artery forming part of the left fourth arch.

degrees and ran upward along the left border of the trachea. Attached to the point of angulation was a stenosed vessel 4 mm. in diameter and 9 mm. in length. This vessel united the left subclavian artery with a diverticulum-like pouch in the anterior wall of the retroesophageal aortic arch. This pouch lay along the left border of the esophagus, and together with the arch, displaced the esophagus anteriad in the form of a semicircle. The pouch also displaced the left border of

the esophagus in a slight curve to the right. The pouch or diverticulum was dome shaped and 25 mm. in diameter at its origin. It projected 15 mm. beyond the anterior surface of the descending arch of the aorta.

Running from this diverticulum (left descending dorsal aortic root) was a second vessel, the ductus Botalli, which ran downward and to the right to reach the pulmonary artery. It was 40 mm. long and 3 mm. in diameter. Its lumen was obliterated. It lay in front of the left main bronchus.

Two centimeters above the origin of the left innominate artery the arch gave off its second branch, the right common carotid artery. This artery was 8 mm. in diameter and lay to the right of the trachea, originating from the aortic arch

Fig. 19. Fig. 20.

Fig. 19.—Photograph of the heart and vessels in Case 6, after dissection by the writer. Note the double aortic arch described under Case 6. The right arch lies behind the trachea and esophagus, and the left arch (left innominate and subclavian artery, isthmus stenosis, and left dorsal root) in front. The ductus arteriosus communicates with the left dorsal root.

Fig. 20.—Specimen in Case 6, viewed from the right side showing the aortic arch behind the trachea and esophagus, with the left arch in front.

where it lay above the right main bronchus. The aortic arch then ran behind the trachea and esophagus, displacing both to the left and especially anteriad. The right bronchus was displaced slightly posteriad by the aortic arch, which rested upon it. The third branch of the aorta was the right subclavian artery which originated 15 mm. above the right carotid. It measured 10 mm. in diameter and lay directly behind the trachea in contact with the right border of the esophagus.

The right recurrent laryngeal nerve ran under the right retroesophageal aorta directly below the right subclavian artery. The left recurrent laryngeal nerve

originated in front of the aortic pouch, and ran beneath and behind it at the attachment of the stenosed isthmus and the ductus Botalli.

After giving off the right subclavian artery the right aortic arch proceeded in a convex curve upward and to the left behind the trachea and esophagus (Fig. 20). It displaced both as already described. It formed a deep bed in the right and posterior wall of the esophagus. Three centimeters to the left of the right subclavian the arch gave off the diverticulum. This pouch, therefore, lay to the left of the spine and to the left of the esophagus. The descending portion of the arch and the thoracic aorta formed a curve around the esophagus and came to lie in contact with the left border of the esophagus. The aorta varied in its caliber in different portions, suggesting syphilitic aortitis. The lower half of the abdominal aorta was firmly attached to the anterior aspect of the spine by a very firm grayish white tumor tissue. The periaortic lymph nodes were infiltrated with tumor tissue.

THE EMBRYOLOGICAL DEVELOPMENT OF THIS ANOMALY

The embryological development of these cases of persistence of the right aortic arch associated with partial occlusion of the left is illustrated

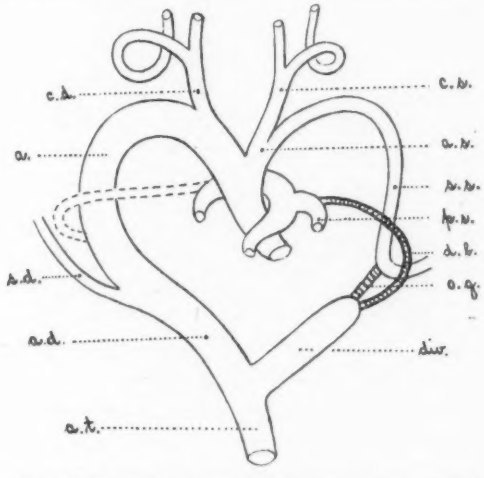

Fig. 21.—Diagram which explains the embryonal development of Cases 1 to 6 inclusive, of total persistence of the right aortic arch and isthmus stenosis of the left aortic arch. The aorta arises from the right fourth arch, the left subclavian and occluded vessel from the left fourth arch. The diverticulum represents the left descending dorsal aortic root.

c.d., right carotid
a., aorta
s.d., right subclavian
a.d., descending aorta
a.t., thoracic aorta
o.g., occluded vessel
c.s., left carotid
a.s., left innominate
s.s., left subclavian
p.s., left pulmonary
d.b., ductus Botalli
div., diverticulum.

in Fig. 21. The right fourth branchial artery together with the right descending dorsal aortic root have formed the aorta, instead of the left. The left fourth arch has developed into the short left innominate artery and the left subclavian so that these are now the first branch of the right-sided aorta. The craniad persisting part of the ascending aorta and the third arch form the carotids on both sides, on the left going off from the left innominate and on the right forming the second branch of the aorta. The right subclavian forms the third branch of the aorta.

Of special interest in our case is the persistence of the left fourth aortic arch as the left subclavian artery and the lateral communicating branch between the fourth arch and the left aortic root (short occluded vessel between the left subclavian and the diverticulum). The diverticulum represents the left descending dorsal aortic root, to which the ductus Botalli is attached. This explanation of the development of our cases makes clear the anatomical and roentgenological findings. The course of the right-sided aorta behind the trachea and esophagus is due to the persistence of the left fourth aortic arch, which forms a tight ring around the trachea and esophagus. The presence of the occluded vessel between the left subclavian artery and the diverticulum causes the aorta to be located to the left and behind the trachea and esophagus instead of on the right side. We really have a condition similar to that found in persistence of both aortic arches, a right totally persistent posterior arch, and a left partially occluded anterior arch (subclavian artery, short occluded vessel and diverticulum).

As in almost all cases of persistence of the right aortic arch, so also, in these cases, the left ductus Botalli persists. The ductus Botalli, which must maintain its communication between the pulmonary artery and aorta during fetal life, holds firmly to its attachment to the aorta, in our cases to the left descending dorsal root. We may look upon this anomaly as an isthmus stenosis of the left fourth arch if we wish to call the occluded vessel or cord between the left subclavian artery and the diverticulum the isthmus of the aorta. Had the left fourth arch not persisted we would have had cases similar to the right-sided aorta with right-sided arch (Fig. 4). Such anatomical specimens have been reported by Versari, Reid, Hoepke, Stibbe, Jaffe, Pense, and others. There is a tendency of a right-sided aorta to remain on the right side, due perhaps to hydromechanical factors, unless the left fourth arch persists and pulls the aorta behind the trachea and esophagus. The embryological development of our cases will be even more clearly visualized by the study of the model of the aortic arches from a human embryo 12.5 mm. long, which Prof. Hochstetter, of Vienna, kindly permitted the writer to reproduce here (Fig. 22).

Congdon has described similar findings in his study of the 13 mm. embryo. The ascending aorta divides into a right and left fourth arch, and the two dorsal aortic roots combine to form the descending thoracic aorta. The left sixth arch forms the ductus arteriosus. This condition of double aortic arch found in the 12 to 13 mm. embryo may persist to form the double aortic arch found after birth. The right arch, usually behind the esophagus and trachea, is often larger than the left arch in front of the trachea. Or, there may develop an isthmus stenosis of the left aortic arch during this early embryological development. In such a case the right aortic arch is forced to persist by the blood current con-

tinuing through the right arch. It is just this condition which I found and explained on an embryological basis in my first case in 1926.

That this explanation was correct has been recently confirmed in the findings at the autopsy of my sixth case, in which I was able to make a perfect anatomical diagnosis from the x-ray and clinical findings. A comparison of the specimens in my Cases 1 and 6 indicate that they represent the same anomaly, which I predicted in 1926 was not rare but had been overlooked.

Blackford two years later proved my contention that obliteration of the left fourth arch, resulting in persistence of the right aortic arch, is related embryologically to coarctation of the aorta of the infantile type. If the left fourth arch becomes stenosed or obliterated after the atrophy of the right fourth arch, then a coarctation of the aorta with its con-

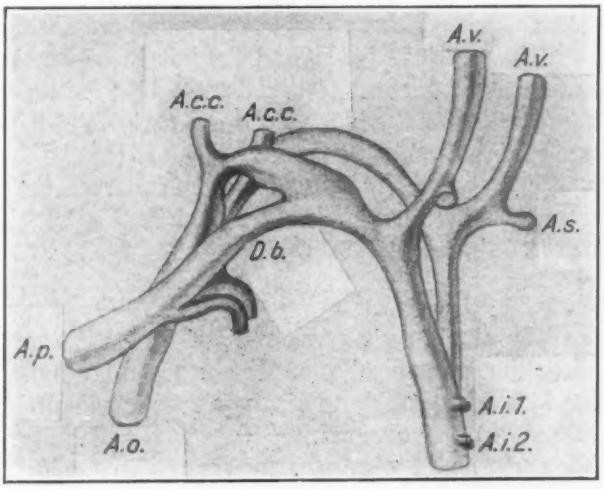

Fig. 22.—Drawing of the large vessels of a 12.5 mm. human embryo made by Professor F. Hochstetter (Anat. Hefte, Vol. 43). This model shows both aortic arches and the ductus Botalli. It is of great value in explaining our case. If the right arch persists and the communication between the left arch and left aortic root becomes occluded, then we have the anomaly described in Cases 1 and 6.

A.p., pulmonary artery
A.o., ascending aorta
D.b., ductus Botalli
A.c.c., common carotid
A.v., vertebral artery
A.s., subclavian artery
A.i.1, first intercostal
A.i.2, second intercostal.

sequent effect upon the heart and circulation must result. In the six cases which I have described, the right aortic arch therefore acts as a safety valve for a stenosis of the left arch in early fetal life. There results a persistence of both aortic arches as in reptiles. The right arch is usually of normal size and runs over the right bronchus and behind the trachea and esophagus; the left arch persists in the form of the left subclavian artery, stenosed vessel or isthmus stenosis, and the diverticulum of the descending thoracic aorta (left descending dorsal root).

In 1930 Sprong and Cutler collected 54 cases of right arch in the anatomical literature; of these 15 were cases of double aortic arch.

Roschdestwensky found 11 of which 3 were the same as Sprong and Cutler's, making 23 cases. Schleussing, Harris and Whitney, Roschdestwensky, Lockhard, Arkin (Case 6), and Snelling and Erb add 6 more cases, making a total of 29 studied anatomically. Arkin adds 4 cases studied clinically and roentgenologically, Blackford 1 case, and Biedermann, also Mardersteig, have reported cases diagnosed roentgenologically. It was Arkin's publication in 1926 which first made the diagnosis possible *intra vitam*. Blackford, Davenport and Bayley have recently gathered 66 cases of right aortic arch from the anatomical and pathological literature. They presented clinical and x-ray findings in a case in a ten-year-old child with a persistence of the right aortic arch accompanied in all probability by a patent ductus arteriosus and interventricular septum defect. There was no autopsy.

It is difficult to explain the persistence of the right aortic arch instead of the normal left arch. We know that both arches are normally present in reptiles, the right arch in birds, and the left in mammals. Perhaps the direction of the blood current is the determining factor, and a slight change in the direction of the blood stream in early fetal life causes the stream to use the right arch more than the left. If that be the case, then we must assume that the direction of blood flow from the pulmonary artery does not change, for we almost always find a left-sided ductus Botalli in cases of right-sided aorta.

DISCUSSION

From the study of these six cases of persistent right aortic arch, as well as the literature on anomalies of the aorta and large arteries, I feel confident that it will be possible to diagnose roentgenologically, and perhaps clinically, still other anomalies.

For clinical and roentgenological purposes the anomalies of the aorta may be classified as follows:

1. *Double aortic arch* (persistence of the right and left aortic arches with patency of both arches).
2. *Right aorta with right-sided arch* (type first described by Assmann).
3. *Right aorta with retroesophageal arch* (type first described roentgenologically and the diagnosis confirmed by Arkin), usually associated with isthmus stenosis of left arch.
4. *Coarctation (isthmus stenosis) of the left aortic arch.*
5. *Absence of part or all of the left aortic arch.*

In *total persistence of both aortic arches* we may expect x-ray findings in the first oblique position resembling those described for right retroesophageal aorta. In addition, a second knob would be visible in front of the trachea. The esophagus would be compressed and displaced forward and to the left; the trachea would have in front of it the other arch. The left or anterior arch is usually smaller than the right: hence

we would expect to find the knob in front of the trachea to be the smaller of the two. They may, however, be of equal size. This anomaly should be easy to recognize since the picture is almost the same as in my six cases.

In *right aorta with right-sided arch,* in which the ascending aorta, arch, and a portion of the descending aorta are all on the right side, we must always look for a left descending aortic root behind the esophagus. This important fact was first emphasized by me in 1926 and recently was confirmed by Blackford, Davenport, and Bayley. This usually forms a diverticulum going off from the left wall of the right-sided descending arch of the aorta. This pouch, which gives off the left subclavian artery and also communicates with the ductus Botalli, produces a forward dislocation of the esophagus which should be easy to recognize in the oblique positions. The esophagus would most likely be dislocated forward, perhaps also to the left. The dislocation would usually be below the level of the aortic knob. A semicircular forward displacement of the esophagus below the level of the right arch would speak for the presence of the left dorsal aortic root behind the esophagus. The subclavian artery may also run behind the esophagus in such cases and could be distinguished by its smaller size. In rare cases, where the diverticulum is very short or absent, the ductus Botalli may be forced to run behind the esophagus to reach the right-sided aorta. In such an event the esophagus would be pushed forward on its left posterior border. It might even be displaced to the right and forward.

In right-sided aorta, or persistence of the right aortic arch, the esophagus may therefore be dislocated by (1) a right-sided aorta with retroesophageal arch, as in my six cases; (2) a diverticulum formed from the left descending dorsal aortic root, as in the type first described by Assmann; (3) a left subclavian artery as the last branch of the right-sided arch; or (4) the ductus Botalli running behind the esophagus.

Another form of so-called dysphagia lusoria or arteria lusoria due to an anomalous right subclavian artery should be mentioned here. This is a type found in cases with a normal left-sided aortic arch. The right subclavian is the last large branch of the aortic arch and hence runs behind (rarely in front of) the esophagus to reach the right side.

In these cases the right subclavian artery may originate as a diverticulum or pouch which represents the right descending dorsal aortic root. This anomalous right subclavian stands in no relation to the ductus Botalli as does the left, hence the abnormal right subclavian has a more variable origin than the left. In 80 per cent of cases collected by Holzapfel the abnormal right subclavian ran behind the esophagus, in 15 per cent between trachea and esophagus, and in 5 per cent in front of the trachea. It is usually located at the level of the second to fourth thoracic vertebrae. X-ray examination of the esophagus should reveal such a vessel in some cases.

The above five types of esophageal displacement (so-called dysphagia lusoria) are of importance because they may cause a dysphagia. They should be of special interest to those who do bronchoscopy and esophagoscopy. The danger of such an examination in any of my six cases of retroesophageal aorta is obvious. It is certainly advisable always to order an x-ray examination of the chest, including the esophagus, before permitting such instrumentation. Of our six cases none had symptoms directly related to the anomalous aorta. The sixth patient had dysphagia, but it was due to a carcinoma of the cardia of the stomach and lower end of the esophagus.

I have discussed these anomalies of the aorta and great vessels in the hope that roentgenologists who have the opportunity of fluoroscoping large numbers of patients will keep them in mind and recognize such cases.

To the clinician I wish also to call attention to certain physical findings which should attract his attention enough to order an x-ray examination for my type of right retroesophageal aorta.

In the six cases I have found the following signs:

1. Dullness on percussion along the right sternal border upward to the head of the right clavicle.
2. Visible systolic pulsation in the second or third right intercostal space near the sternum, or in the right supraclavicular fossa.
3. Palpable strong pulsation in right supraclavicular fossa.
4. Maximum intensity of the aortic heart sounds to the right and above the usual location. (Often in the right supraclavicular fossa.)
5. Displacement of the trachea slightly to the left.
6. Tracheal tug.
7. Delay in the passage of a rigid stomach tube at the level of the third dorsal vertebra with pulsation transmitted along the tube.

It is not to be expected that all of these signs will be positive in every case. In my six cases the heart presented normal findings in all; there was no clinical or post-mortem evidence (in two cases) of cardiac anomalies. The electrocardiograms obtained in four of the cases were normal. Aortic anomalies frequently occur in the absence of cardiac malformations. Theoretically, accurate timing of the pulsation in the carotid and subclavian arteries should also be of value in the diagnosis of some of the anomalies we have discussed. For example, in my type of double aortic arch a left innominate usually forms the first large branch of the aorta, followed by the right carotid and right subclavian. In anomalous right subclavian artery arising from the descending aorta the pulsation in the subclavian should also be slightly delayed.

CONCLUSIONS

Six cases of a clinically new aortic anomaly are presented, two with post-mortem findings. This consists of a total persistence of the right

aortic arch, combined with a persistence of the left aortic arch in the form of the left subclavian artery, an isthmus stenosis, and a diverticulum of the aortic arch (left descending dorsal aortic root). In other words, we have here a persistence of both aortic arches as in reptiles. The right arch lies behind the esophagus, and the left arch in front of the trachea.

The cases all present characteristic x-ray findings which are: (1) a shadow to the right of the sternum, running upward to the head of the right clavicle, with a distinct systolic pulsation; (2) slight displacement of the trachea, and definite displacement of the esophagus to the left; (3) absence of the normal aortic knob on the left side, or only a small shadow of the descending arch on the left side; in some cases two aortic knobs, one on each side; (4) in the right oblique position the aortic knob lies behind the trachea and esophagus, both of which are displaced forward and to the left (most characteristic of all is the circular forward displacement of the esophagus by the arch of the aorta); (5) shadow of the diverticulum either in the retroesophageal knob or in the shadow of the descending arch on the left side; (6) in the left oblique position a wide shadow of the ascending aorta to the right of the trachea and evidence that the aortic arch runs behind the esophagus to reach the left side.

The first case was diagnosed in 1925 and confirmed at autopsy. Since that time five additional cases have been diagnosed and are described. The last case was recognized clinically and the diagnosis confirmed by x-ray examination and autopsy. In this case a complete anatomical diagnosis was made with the aid of the roentgen ray.

The following clinical signs were found in the six cases: (1) dullness to the right of the sternum, (2) visible systolic pulsation in the second and third right intercostal spaces, (3) palpable, strong pulsation in the right supraclavicular fossa, (4) maximum intensity of the aortic sounds in the region of the head of the right clavicle, (5) slight displacement of the trachea to the left, (6) tracheal tug, (7) delay in passage of the stomach tube at the level of the third dorsal vertebra, with transmitted pulsation from the arch of the aorta.

Attention is called to the presence of aortic anomalies without any cardiac malformations and in many cases without clinical symptoms. The embryological development and clinical significance of this new clinical and x-ray picture are discussed. Suggestions are given for the recognition of still other anomalies of the aorta and its large branches. The great importance of examination of the esophagus in anomalies of the aorta is stressed.

REFERENCES

Abbott, M. E.: Right Aortic Arch, in Osler and McCrae, Modern Medicine, ed 3, Philadelphia, 1927, Lea & Febiger, 4: p. 790.

Arkin, Aaron: Totale Persistenz des rechten Aortenbogens im Röntgenbild, Wien. Arch. f. inn. Med. 12: 385, 1926.

Assmann, Herbert: Klinische Röntgendiagnostik der inneren Erkrankungen, ed. 3, Leipzig, 1924, F. C. W. Vogel, p. 103.
Biedermann, F.: Der rechtseitige Aortenbogen im Röntgenbild, Fortschr. a. d. Geb. d. Röntgenstrahlen **43**: 168, 1931.
Blackford, L. M.: Coaretation of the Aorta, Arch. Int. Med. **41**: 702, 1928.
Blackford, L. M., Davenport, T. F., and Bayley, R. H.: Right Aortic Arch, Am. J. Dis. Child **44**: 823, 1932.
Blackhall, Morison, A.: Cardiac Malformation With Vascular Anomalies, J. Anat. **62**: 227, 1928.
Congdon, E. D.: Transformation of the Aortic Arch System During the Development of the Human Embryo, Contrib. Embryol. No. 14, Carnegie Inst., Washington, 1922, p. 47.
Goldbloom, A. A.: The Anomalous Right Subclavian Artery and Its Possible Clinical Significance, Surg. Gynec. Obst. **34**: 378, 1922.
Grossmann, J., and Meller, O.: Hohe Rechtslage der aorta bei normal gelagertem Herzen in einem Fall von Situs viscerum inversus subdiaphragmaticus, Fortschr. a. d. Geb. d. Röntgenstrahlen **33**: 1120, 1928.
Hamdi: Eine seltene Aortenanomalie, Deutsche med. Wchnschr. **2**: 1410, 1906.
Hermann, W. W.: Double Aortic Arch, Arch. Path. **6**: 418, 1928.
Herrnheiser: Pulmonalstenose mit hoher Rechtslage der Aorta, Fortschr. a. d. Geb. d. Röntgenstrahlen **29**: 519, 1922.
Harris, H. A., and Whitney, C. E.: The Heart of a Child, Aged 19 Months, Presenting Right and Left Aortic Arches, With Multiple Anomalies of the Heart and Great Vessels, Anat. Rec. **34**: 221, 1927.
Herxheimer, G.: Missbildungen des Herzens und der grossen Gefässe, Ernst Schwalbe, die Morphologie der Missbildungen des Menschen und der Tiere, Part III, Section 2, Chapter 4, Jena, 1910.
Herzog, F., and Firnbacher, E.: Beitrag zu den Anomalien der Aorta und des Oesophagus, Fortschr. a. d. Geb. der Röntgenstrahlen **35**: 1236, 1927.
Hoepke, Hermann: Ueber eine Varietät des Aortenbogens, Anat. Anz. **54**: 60, 1921.
Holzapfel, G.: Ungewöhnlicher Verlauf der Arteria subclavia dextra, Anatom. Hefte, Part I, **12**: 369, 1899.
Jaffe, Karl: Ein Fall von Missbildung des Herzens und der Gefässe, Inaug. Diss., Leipzig, Munich, 1921, J. F. Bergmann.
Lockhard, R. D.: Complete Double Aortic Arch, J. Anat. **64**: 189, 1930.
Löweneck, M.: Einige seltene Beobachtungen aus der Oesophagus-Pathologie, Fortschr. a. d. Geb. d. Röntgenstrahlen **35**: 1230, 1926.
Mardersteig, Klaus: Persistenz des rechtseitigen Aortenbogens im Röntgenbild, Fortschr. a. d. Geb. der Röntgenstrahlen **44**: 163, 1931.
Pense, Gertrud: Ein Fall von rechtsseitigem aortenbogen und seine entwicklungsgeschichtliche Deutung, Anat. Anz. **70**: 257, 1930.
Reid, D. G.: Three Examples of a Right Aortic Arch, J. Anat. and Physiol. **48**: 174, 1914.
Roschdestwensky, K. G.: Der doppelte aortenbogen, Anat. Anz. **68**: 145, 1929.
Saupe, Erich: Ueber Dysphagia lusoria, Fortschr. a. d. Geb. d. Röntgenstrahlen **33**: 740, 1925.
Schleussing, Hans: Beiträge zu den Missbildungen des Herzens, Virchows Arch. f. path. Anat. **254**: 579, 1925.
Snelling and Erb: Double Aortic Arch, Arch. Dis. Child. **8**: 401, 1933.
Spitzer, A.: Ueber den Bauplan des normalen und missbildeten Herzens, Virchows Arch. f. path. Anat. **243**: 81, 1923.
Sprong, D. H., and Cutler, N. L.: A Case of Human Right Aorta, Anat. Rec. **45**: 365, 1930.
Stibbe, E. P.: True Congenital Diverticulum of the Trachea in a Subject Showing Also Right Aortic Arch, J. Anat. **64**: 62, 1929.
Wheeler, Digby, and Abbott, M. E.: Double Aortic Arch and Pulmonary Atresia, With Pulmonic Circulation Maintained Through a Persistent Left Aortic Root, Canad. M. A. J. **19**: 297, 1928.

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THE VELOCITY OF THE BLOOD FLOW IN THERAPEUTIC HYPERPYREXIA*

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IT IS the purpose of this communication to report the results of a study of the effect of artificial fever produced by diathermy, electric blanket, and typhoid vaccine upon the velocity of blood flow as determined by the decholin method in two patients, one with an apparently normal heart, and the second with syphilitic heart disease. Treatment of patients with general paresis by these means afforded the opportunity for these studies.

Various observers[1, 2, 3] have already shown that in exercise and hyperthyroidism, with an increase in the body metabolism, an increase in the velocity of the blood flow occurs. Kissin and Bierman[4] have recently shown that therapeutic fever produced by the radiotherm likewise causes an increase in the velocity of the blood flow. It was felt that repeated determinations of the velocity of the blood flow on the same patient as fever therapy continued might be of interest, enabling one to note (a) residual effects if any upon the basal velocity of blood flow and (b) the velocity of flow for different temperature levels.

Subjects.—Observations were made upon two patients: Patient 1, S. C., aged thirty-two years; height 67 inches; weight 120-125 pounds. Diagnosis: General paresis. There were no signs or symptoms of cardiac pathology. Patient 2, M. M., aged forty-four years; height 67 inches; weight 164-170 pounds. Diagnosis: General paresis, syphilitic heart disease with cardiac hypertrophy and aortic insufficiency, and hematuria of unknown origin. There were no signs or symptoms of cardiac decompensation.

Methods.—The method of Winternitz[5] as modified by Gargill[2] was used to determine the arm-to-tongue velocity flow. From 3 to 4 c.c. of 20 per cent decholin (sodium dehydrocholate) solution were injected into the median cubital vein as rapidly as possible (usually within less than one second), the duration of the injection being noted with a stop watch. The time elapsing from the end of the injection to the onset of a bitter taste was also noted and considered the "real arm-to-tongue time."[2] The pathway traversed by the decholin is as follows: from the right elbow to the right side of the heart, to the lungs, the left side of the heart, the internal carotid artery and then to the tongue.

The method of inducing hyperpyrexia by means of diathermy has been described by others.[6] In this clinic, however, segmented electrodes encircling the waist, the upper arms, and the thighs are used and are applied with care not to cause any vascular constriction. The right arm electrode was loosened before each injection of decholin. As insulating covering, a large celotex box containing eight 60-watt

*From the Neurosyphilis Clinic of the Boston Psychopathic Hospital under the direction of Dr. Harry G. Solomon, Chief of Therapeutic Research.

electric bulbs completely encloses the patient (with the exception of the head). The patient's movements are relatively unrestricted. Three doors in the box permit manipulations of the patient. The dry and wet bulb temperatures of the air blanket within the insulating box rise rapidly as treatment continues, and, since very little circulation of air occurs, air blankets of different temperatures are present as one proceeds from body level to the roof of the box. Dry and wet bulb levels of about 105° and 120° F., respectively, are obtained in about one hour, fifteen inches above body level.

Fever induction by means of the electric blanket did not differ from the method described by Wilgus and Lurie.[7] Typhoid vaccine fever was induced by the intravenous injection of from 125 to 1,250 million bacteria.

Patient S. C. received five diathermy treatments, six electric blanket treatments, and three intravenous typhoid vaccine shocks, totaling fourteen fever treatments over a period of four weeks. Patient M. M. was given eleven diathermy treatments over a period of six weeks.

In each instance observations were made on the patient under basal conditions before fever was induced. Following a period of from twenty to forty minutes during which the pulse rate and blood pressure were observed every five minutes, a single observation of the blood velocity and occasionally a second determination was made. The duplicate determinations invariably checked within two seconds. These values for blood velocity flow and average values of the blood pressure levels and of the pulse rates during the rest period were used as basal values for the experiment. Fever treatment was then started and velocity rates determined with temperature rising, at a stationary level, and falling. Rates were obtained during the typhoid chill. Pulse rates were counted for twenty to thirty seconds during the velocity determinations. Blood pressures were taken immediately before or after, and body temperature at the time of the test. Rectal temperatures, recorded by means of a self-recording Leeds-Northrup temperature unit inserted during the entire treatment, were used in all experiments except in the electric blanket treatment. In the latter experiments mouth temperatures were used since only slight differences have been found between oral and rectal readings in this type of fever.

RESULTS

Basal Velocity Rates.—Sixteen basal velocity determinations were obtained on S. C., whose heart was normal to examination before the induction of fever on fourteen treatment days (Fig. 1). The basal arm-to-tongue velocity rates varied from 18 to 9.5 seconds and tended to increase during the later days of the fever treatments. The changes in the velocity of the blood flow were accompanied by parallel changes in other clinical findings, the basal pulse rate varying from 56 to 80 per minute, the body temperature from 96.7° to 99.3°, the diastolic pressure from 47 to 63 mm. mercury, the systolic pressure from 82 to 98 mm. mercury, and the pulse pressure from 30 to 41 mm. mercury.

Eleven basal velocity rates were obtained on M. M., who showed evidences of luetic heart disease, on eleven treatment days and ranged from 20.2 to 14.6 seconds (Fig. 2). The velocity rates of this patient also tended to increase as fever therapy continued but were accompanied by changes in other clinical findings which did not parallel

the changes in the basal velocity of the blood flow. The basal pulse rate was slowed as fever therapy was repeated, ranging from 83 to 58 per minute; the body temperature varied from 96.5° to 98.8°; the

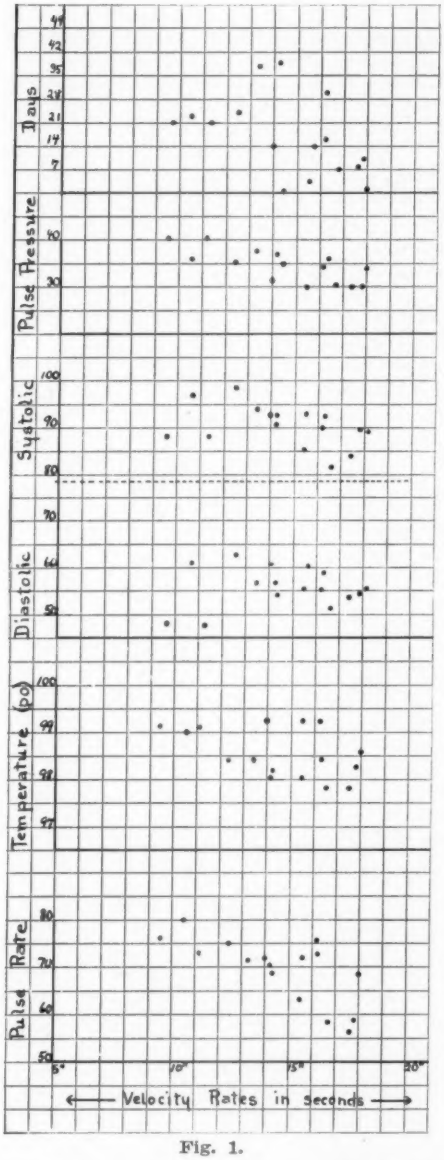

Fig. 1.

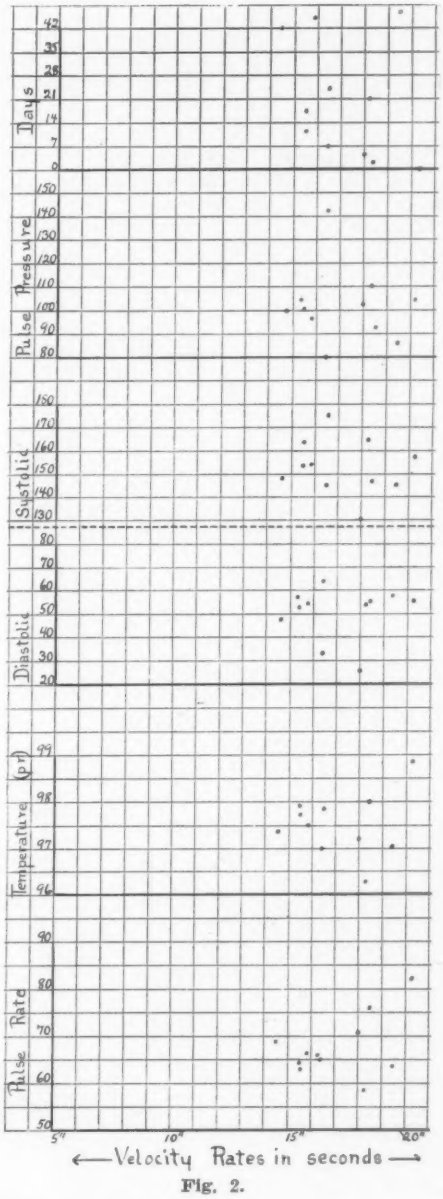

Fig. 2.

Fig. 1.—Velocity rates under basal conditions (Patient S. C.).
Fig. 2.—Velocity rates under basal conditions (Patient M. M.).

diastolic pressure, from 25 to 65 mm. mercury; the systolic pressure, from 130 to 175 mm. mercury, and the pulse pressure, from 80 to 143 mm. mercury.

A comparison of the basal velocity rates obtained on both patients reveals more marked changes in those of the patient with an apparently normal heart, S. C. In both patients a hastening of the basal

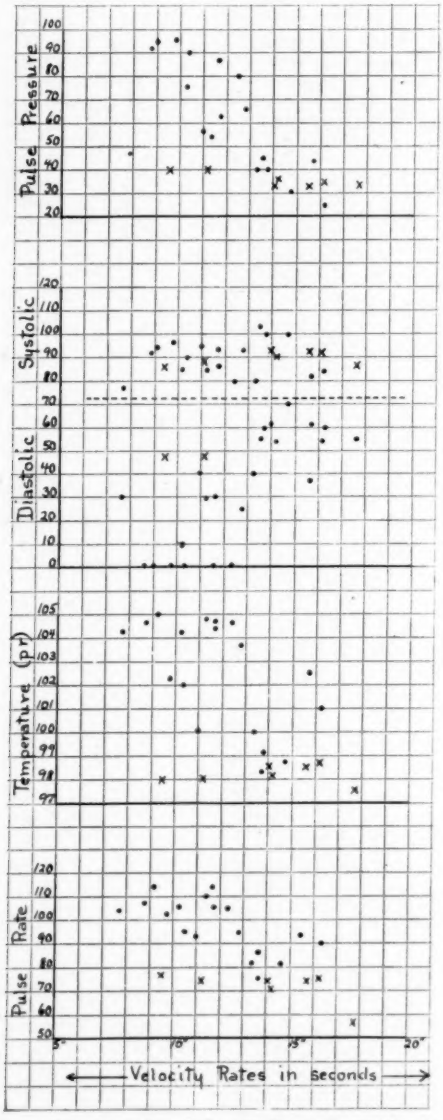

Fig. 3.—Velocity rates in fever produced by diathermy (Patient S. C.). "×" equals basal rates included for comparison.

flow occurred as fever therapy continued, accompanied by an increase in the pulse rate of S. C., but by a slowing of the pulse rate of the patient with luetic heart disease. The basal velocity rates of S. C. show a linear relationship best to the pulse rate; those of M. M. also to the pulse rate, but an inverse one.

Velocity Rates During Fever.—During the induced fevers fifty arm-to-tongue velocity determinations were obtained on S. C. and consisted of the following: 18, 17, and 15 determinations during diathermy,

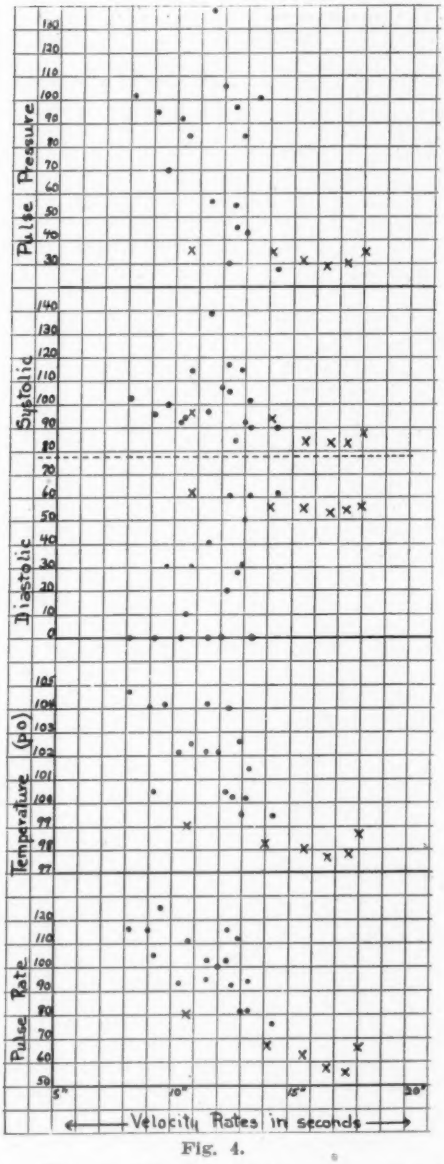

Fig. 4.

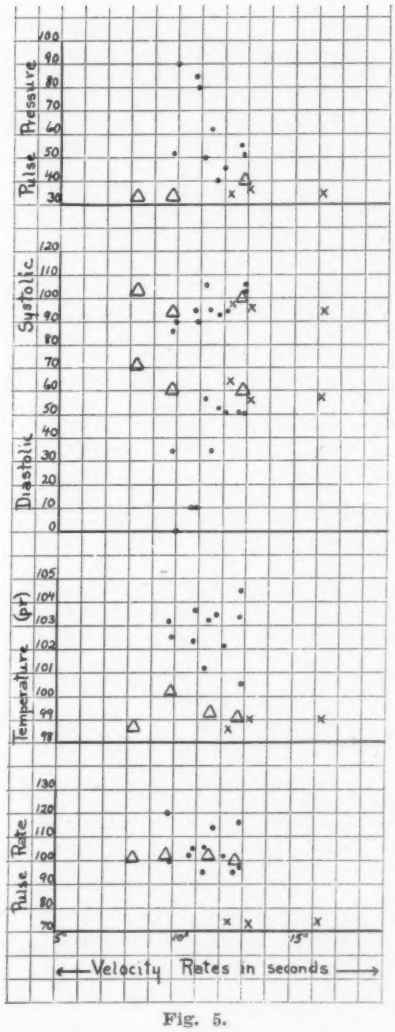

Fig. 5.

Fig. 4.—Velocity rates in fever produced by electric blanket (Patient S. C.). "×" equals basal rates included for comparison.

Fig. 5.—Velocity rates in fever produced by protein shock (typhoid) (Patient S. C.). "×" equals basal rates; △, chills.

electric blanket therapy, and typhoid vaccine fever, respectively (Figs. 3, 4, and 5). An increase in the velocity of flow occurred at

all times, with but one exception, as body temperature was rising. With a fall in body temperature the velocity of flow was less rapid than at a similar level when body temperature was rising, on some occasions slower than the basal level obtained before fever therapy was started even though body temperature was four degrees above the basal level. Variations in the velocity rates of six seconds were present for similar pulse and temperature levels. No absolute relationship could be found between the percentage increases in the velocity of blood flow and other clinical findings. During diathermy fever, however, a suggestive linear relationship is best seen between the velocity of the blood flow and the pulse rate, less so between the velocity of flow and the pulse pressure. In fever induced by the electric blanket, a similar relationship is apparent between the velocity of flow and the pulse level, less so between velocity of flow and the body temperature. The determinations obtained during typhoid vaccine fever show less variation, and the percentage increases in the velocity of flow are less marked for equal rises of body temperature than occur during diathermy and electric blanket fever. The changes in other clinical findings such as systolic, diastolic, and pulse pressures and pulse rate are also less marked for this type of induced fever.

The four velocity rates obtained on S. C., during the chill following the intravenous injection of typhoid vaccine are of considerable interest. Table I shows the percentage deviations from basal conditions occurring at this time. The pulse rate is increased from 33 to 41 per cent. The velocity of the blood flow, however, increased from 6 to 50 per cent above basal conditions. The percentage deviations of the velocity of flow and of pulse rate do not run exactly parallel but do show a closer relationship than that found between the velocity of flow and other clinical findings.

Twenty velocity determinations were obtained on M. M. during diathermy fever (Fig. 6). An increase in the velocity of blood flow

TABLE I

DEVIATIONS FROM BASAL CONDITIONS DURING TYPHOID VACCINE CHILL

	EXPERIMENT I		EXPERIMENT II	
	OBSERVATIONS			
	I	II	I	II
Velocity rate	50%	6%	4%	28%
Pulse rate	33%	35%	39%	41%
Pulse pressure	0	–*	2%	–12%
Systolic pressure	6%	–	4%	– 2%
Diastolic pressure	9%	–	5%	5%
Body temperature (p.o.)	0.2° F.	–	0	2° F.
Body temperature (p.r.)	0.1° F.	0.5° F.	0.1° F.	1.2° F.

*No observations made.

occurred always when body temperature was above basal level with but one exception—when the body temperature was falling. The results obtained reveal also less marked increases as the body temperature was falling than when rising and bore no absolute relationship to other clinical findings. Variations in the velocity time of as much as seven seconds were obtained for similar temperature levels.

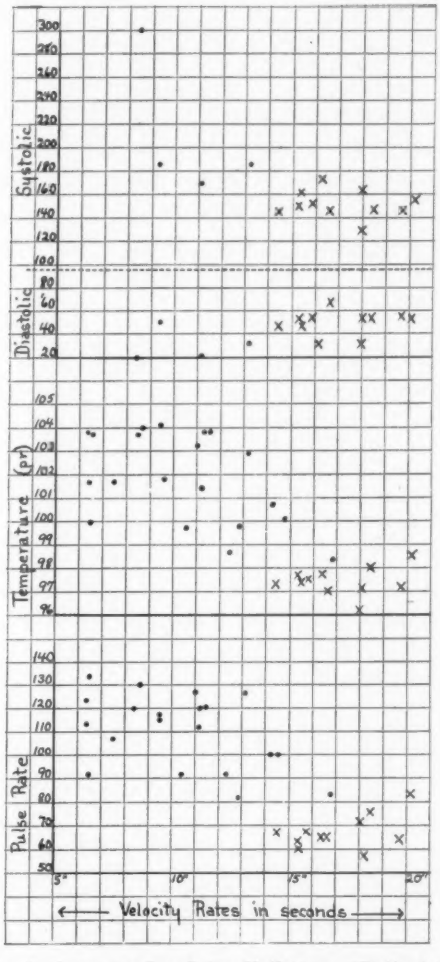

Fig. 6.—Velocity rates in fever produced by diathermy (Patient M. M.). "×" equals basal rates included for comparison.

A comparison of the average velocity rates and other clinical findings obtained on both patients during diathermy fever reveals more marked changes in the velocity of flow and pulse rate of the patient with luetic heart disease, M. M., than of the patient with no cardiac pathology. This is seen in Table II.

With the induction of therapeutic fever in each patient there occurred, as a rule, a drop in the diastolic blood pressure frequently

TABLE II

A COMPARISON OF THE INCREASES IN THE PULSE RATE, BODY TEMPERATURE, AND VELOCITY OF BLOOD FLOW DURING DIATHERMY FEVER

(BASED ON AVERAGE VALUES)

	BEFORE FEVER			DURING FEVER			INCREASE		
	PULSE	BODY TEMP.	VELOCITY	PULSE	BODY TEMP.	VELOCITY	PULSE	TEMP.	VELOCITY
S. C.	71	98.3° F.	14.8″	111	104.8°	10.2″	56%	6.5°	45%
M. M.*	65	97.5° F.	16.7″	124	103.8°	8.8″	91%	6.3°	90%

*Patient with luetic heart disease.

approaching zero, and a slight rise in the systolic blood pressure with a resulting increase in the pulse pressure. Not many blood pressure readings were obtained during fever treatment of the patient with luetic heart disease, but on one occasion the pulse pressure increased from a basal level of 100 mm. mercury to a level of 280 mm. mercury at 103° F.

DISCUSSION

The individual variations in the basal velocity of the blood flow as shown by the repeated results on the two patients undergoing therapeutic fever are greater than those obtained by other workers on normal patients. Blumgart and Weiss[8] determined the basal velocity of blood flow on fifty-three normal patients by the radioactive method and found variations of from four to five seconds only on two patients on repeated tests. Tarr and his coworkers[9] utilizing the decholin procedure found individual variations of only three seconds on a group of sixty normal men and women. Robb and Weiss[10] made from three to eight determinations of the circulation time by means of the sodium cyanide method on the same day on a group of eight patients and found variations, as a rule, of two seconds or less. On three subjects variations of three and four seconds were obtained and were attributed to restlessness during the test. Though it has been shown by the above named workers that interindividual variations in the basal velocity of blood flow are fairly large, as much as twelve seconds, no conclusions can be drawn as to variations in any one individual over a lengthy time interval, i.e., days or weeks. Search of the literature has not revealed any work done along these lines.

The following factors can be considered as possibly responsible for the greater-than-normal variations of the basal blood flow in M. M. and S. C. during their course of therapeutic fever.

a. Changes in the basal metabolic rate due to repeated therapeutic fever altering the basal velocity of blood flow.

b. Emotional factors accompanying the test altering the metabolic rate.

c. Myocardial changes as a result of therapeutic fever.

The constancy of the basal metabolic rate, allowing for plus or minus 10 per cent individual variations, is a well-established fact.[11] Basal metabolic rates were determined frequently (80 determinations) upon a patient in this clinic who had been given fifty diathermy treatments consisting of about 250 hours of diathermy fever over a period of seven months, and it was apparent that repeated diathermy fever therapy had no residual effect upon the basal metabolic rate (unpublished data).

The increase in pulse rate and velocity flow of the normal patient during the latter half of his treatments may indicate an increase in metabolic rate due not to therapeutic fever but to uncontrolled factors, such as increased muscle tension and emotion, in spite of evident basal conditions. These factors, especially the latter, tend to raise the pulse level and the basal metabolic rate.[12] Landis,[13] however, concluded that emotional conditions do not necessarily affect the metabolic rate. The changes in metabolic rate which did occur during "emotion" and "upset" experiments Landis attributed partly to muscular activity, but for the most part to vascular changes involving the volume flow of blood. Segal and his coworkers[14] found little or no change in the basal metabolic rate as a result of emotion in a group of normal patients. It appears rather illogical to assume that S. C. became more tense or "upset" emotionally as treatments were repeated since experience shows that patients tend to become accustomed to the procedure. In addition, it appears that the variable velocity rates obtained on this patient require an explanation depending on factors other than the basal metabolic rate since a basal pulse rate from 71 to 73 per minute, suggesting a fairly fixed metabolic rate, showed variations in six velocity rates of from 11.1 to 16.2 seconds.

It is improbable that therapeutic fever as used in this clinic should cause myocardial damage, and experience in a large group of cases indicates that damage does not occur. Damage to heart muscle should manifest itself by an increase in basal pulse rate (damage to the neuromuscular bundle would slow the heart) and by a slowing of the basal velocity of blood flow. In neither patient were these two findings present together as treatment continued. The upper limits of temperature in therapeutic fever as carried out on these two patients are at a level at which no destruction of muscle tissue occurs. Therapeutic fever in itself possesses no toxic effect. Repeated fever therapy given to M. M., the cardiac patient, caused a slowing of pulse rate and an increase in velocity flow as treatment continued, changes which resemble closely the stimulating effect of digitalis therapy upon a failing myocardium.[15] The first few basal velocity rates on this pa-

tient were slower than the normal rates obtained by Gargill[2] and Tarr and his coworkers[9] in their series by the decholin procedure, and Blumgart and Weiss[16] have shown that in luetic heart disease with aortic regurgitation a slow velocity rate may be the precursor of a failing heart even before any subjective symptoms occur.

The changes in basal pulse rates and velocity of flow in both patients are, therefore, not due to residual effects of therapeutic fever upon the basal metabolic rate or to myocardial damage but are probably the results of a specific effect of therapeutic fever upon the cardiovascular system, resulting among other things in better heart muscle tone.

The variations in the velocity of the blood flow of each patient at different temperature levels during therapeutic fever may be due to (a) fluctuations in the metabolic rate occurring at these temperature levels,[17] or (b) variable changes in the cardiovascular system (changes in blood volume and viscosity, differences in blood pressure levels, etc.), especially brought on by changes in the wet bulb temperatures of the enveloping air blanket.[18] The less marked increases in the velocity of flow which occur as the body temperature is falling resemble in a way the metabolic rate, the metabolic rate for similar temperature levels during therapeutic fever being less when the body temperature is falling than when rising.[17] The increases in the velocity of the blood flow obtained in the above reported experiments are less marked than those obtained by Kissin and Bierman[4] by the sodium cyanide method on a group of patients undergoing radiotherm hyperpyrexia. The reason for this is not apparent.

The smaller increases in the velocity of flow occurring during fever induced by typhoid vaccine in S. C. may be due to the absence of the hot, moist, insulating air blanket present in diathermy and electric blanket fever and its effect upon the peripheral blood flow. Hewlett[19] has shown that, when perspiration occurs on exposure to increased environmental temperatures, the peripheral circulation, approximating about 30 per cent of the total circulation at this time, is increased as much as 400 per cent and influences the general circulation considerably. These conditions exist during diathermy and electric blanket fever in which the surrounding air temperature is high (120° to 135° F.) and diaphoresis is quite rapid and marked. During typhoid vaccine fever, however, the peripheral circulation is slowed as body temperature is rising and increased above normal as it falls.[19] The marked differences occurring in the peripheral blood flow during diathermy and electric blanket fever, on the one hand, and typhoid vaccine, on the other, may explain the less marked increases in the velocity of blood flow occurring during the latter type

of induced fever. The smaller increases in the velocity of flow during typhoid vaccine fever cannot be explained by differences in the metabolic rate since it has been found that the rises in metabolic rate for these three types of induced fever (excluding the typhoid vaccine chill) are nearly the same.[17]

Barr and his coworkers[20] have shown that during the typhoid chill a marked increase in basal metabolic rate ranging up to 200 per cent occurs. Metabolic rates determined upon a patient in this clinic during the typhoid chill ranged from 125 to 180 per cent above normal. The pulse rates obtained on S. C. during the chill are in no way indicative of this great rise in metabolism. The percentage increases in the velocity of blood flow also do not parallel the increase in metabolic rate, the latter finding being contrary to the findings on patients with thyrotoxicosis by Blumgart and his coworkers,[3] who found the increase of the velocity of pulmonary blood flow proportional to the height of metabolic rate. Their results showed that an average increase of 33 per cent in metabolic rate was accompanied by an average increase of 61 per cent in the arm-to-arm blood flow. The arm-to-arm circuit (arm-to-heart circuit plus the pulmonary circuit) utilized by Blumgart and his associates is about equal in distance to the arm-to-tongue pathway utilized in the decholin procedure, and a fairly good comparison can be made. The percentage increase in the velocity of flow over the arm-to-tongue pathway during the typhoid chill at a period when the increase in metabolic rate is from 100 to 200 per cent above basal conditions is less than the percentage increase found by Blumgart and his coworkers in the arm-to-arm velocity time at a much lower metabolic level in thyrotoxicosis. This difference may be due to the increased peripheral blood flow occurring in thyrotoxicosis[21] as opposed to the diminished peripheral flow occuring during the chill of typhoid vaccine.[19]

The more rapid pulse and velocity rates obtained on the patient with luetic heart disease during diathermy fever when compared with those of the patient without cardiac disease may be explained by the observation that patients with organic heart disease require more oxygen to perform a given amount of work than do patients with normal hearts.[22] Metabolic rates obtained on a group of patients in this clinic during diathermy fever revealed a greater increase in metabolism for a given rise in body temperature when heart disease was present than when absent (unpublished data). That the velocity of blood flow during fever is a better index of cardiac stress than the pulse rate is shown by the following:

a. In a well-compensated patient with aortic insufficiency, cardiac hypertrophy, and general paresis, a temperature of 104° to 104.8° F.

(R) was accompanied by an increase in pulse rate from 69 to only 94 per minute, even with marked discomfort of the patient. The velocity of blood flow showed increases as high as 95 per cent above basal level.

b. A second patient with general paresis and no apparent heart disease who tolerated a temperature of 104.8° to 105.8° F. (R) with a minimum of discomfort, showed an increase in pulse rate from a basal level of 75 to 124 per minute, with the velocity of blood flow showing an increase of only 40 to 54 per cent. Though the pulse rate of the patient with luetic heart disease showed an increase of only 36 per cent, the velocity of flow increased as much as 95 per cent, whereas an increase in pulse rate of 65 per cent in the patient without heart disease was accompanied by an increase of only 40 to 54 per cent in the velocity of blood flow.

It has already been shown that there is a disproportionate increase in pulse rate and velocity of flow for nearly similar rises in body temperature between the patient evidently free from heart pathology and the one with luetic aortic insufficiency and cardiac hypertrophy. The response of the heart in therapeutic fever as shown by changes in the blood pressure, pulse rate, and velocity of flow will no doubt depend largely upon the functional capacity of the heart. It appears, then, that the responses of the cardiovascular system to therapeutic fever, induced either by diathermy or the electric blanket, can be used as an index of the capacity of the heart to respond to conditions of stress. The functional efficiency and reserve of the heart can be estimated by inducing a rise in body temperature to some arbitrary level (100° to 102° F.) under basal conditions and noting the changes in the cardiovascular system which occur. A comparison of the changes in the basal metabolic rate and the cardiovascular system (systolic, diastolic and pulse pressures and especially the velocity of the blood flow) with those obtained before fever therapy should enable one to estimate the heart capacity and reserve. Repeated tests during the evolution of any underlying heart pathology would allow an estimate of the direction in which the efficiency of the heart was proceeding.

SUMMARY AND CONCLUSIONS

Therapeutic fever was induced by means of diathermy, electric blanket, and typhoid vaccine in two patients with general paresis, one apparently free from heart disease, the second with luetic aortic regurgitation and cardiac hypertrophy, and the arm-to-tongue velocity time determined by the decholin method.

During the second half of the fever treatments of the patient with an apparently normal heart an increase in the basal velocity of flow

occurred and was accompanied by an increase in the pulse rate. The basal velocity of blood flow of the patient with luetic heart disease tended also to increase as fever therapy continued but was accompanied by a slowing in the pulse rate.

The conclusion is suggested that the changes in the basal velocity of blood flow and pulse rates of both patients are due to the beneficial effects of therapeutic fever upon the myocardium, the changes in the patient with luetic heart disease resembling those characteristic of digitalis therapy.

Therapeutic fever caused an increase in the velocity of the blood flow in both patients, but no absolute quantitative relationship was found between the percentage increases in the velocity of flow and the degree of temperature rise. The increases in the velocity of flow were least marked during typhoid vaccine fever.

Based on average values for nearly similar rises in body temperature in diathermy fever, the increase in the velocity of the blood flow of the patient with luetic heart disease was much greater than that of the patient with an apparently normal heart.

The response of the cardiovascular system to induced fever is proposed as a new test of cardiac function and reserve.

REFERENCES

1. Ellis, L. B.: Circulatory Adjustments of Moderate Exercise in Normal Individuals With Particular Reference to Interrelation Between Velocity and Volume of Blood Flow, Am. J. Physiol. **101**: 494, 1932.
2. Gargill, S. L.: Use of Sodium Dehydrocholate as Clinical Test of Velocity of Blood Flow, New England J. Med. **209**: 1089, 1933.
3. Blumgart, H. L., Gargill, S. L., and Gilligan, D. R.: Studies on the Velocity of Blood Flow: XIII. The Circulatory Response to Thyrotoxicosis, J. Clin. Investigation **9**: 69, 1930.
4. Kissin, M., and Bierman, W.: Influence of Hyperpyrexia on Velocity of Blood Flow, Proc. Soc. Exper. Biol. & Med. **30**: 527, 1933.
5. Winternitz, M., Deutsch, J., and Brüll, Z.: Eine klinisch brauchbare Bestimmungsmethode der Blutumlaufszeit mittels Decholininjektion, Med. Klin. **27**: 986, 1931.
6. Neymann, C. A., and Osborne, S. L.: Artificial Fever Produced by High Frequency Currents: Preliminary Report, Illinois M. J. **56**: 199, 1929.
7. Wilgus, S. D., and Lurie, L.: The Fever Treatment of Paresis by Means of the Diathermy Current and the Electric Blanket, Illinois M. J. **60**: 341, 1931.
8. Blumgart, H. L., and Weiss, S.: Studies on Velocity of Blood Flow: II. The Velocity of Blood Flow in Normal Resting Individuals, and a Critique of the Method Used, J. Clin. Investigation **4**: 15, 1927.
9. Tarr, L., Oppenheimer, B. S., and Sager, R. V.: Circulation Time in Various Clinical Conditions Determined by Use of Sodium Dehydrocholate, AM. HEART J. **8**: 766, 1933.
10. Robb, G. P., and Weiss, S.: A Method for Measurement of Velocity of Pulmonary and Peripheral Venous Blood Flow in Man, AM. HEART J. **8**: 650, 1933.
11. Du Bois, E. F.: Basal Metabolism in Health and Disease, Philadelphia, 1924, Lea & Febiger, p. 110.
12. Idem: Ibid., pp. 352 and 353.
13. Landis, C. L.: Studies on Emotional Reactions: IV. Metabolic Rate, Am. J. Physiol. **74**: 188, 1925.
14. Segal, H. L., Binswanger, H. F., and Strouse, S.: The Effect of Emotion on Basal Metabolism, Arch. Int. Med. **41**: 834, 1928.

15. Weiss, S., and Blumgart, H. L.: The Effect of the Digitalis Bodies on the Velocity of Blood Flow Through the Lungs and on Other Aspects of the Circulation: A Study of Normal Subjects and Patients With Cardiovascular Disease, J. Clin. Investigation **7**: 11, 1929.
16. Blumgart, H. L., and Weiss, S.: Studies on Velocity of Blood Flow: III. The Velocity of Blood Flow and Its Relation to Other Aspects of the Circulation in Patients With Rheumatic and Syphilitic Heart Disease, J. Clin. Investigation **4**: 149, 1927.
17. Kopp, I.: Metabolic Rates in Therapeutic Fever, Am. J. M. Sc. **190**: 491, 1935.
18. Barbour, H. G., Dawson, M. H., and Neuwirth, I.: Heat Regulation and Water Exchange: X. Water, Salt and Lipoid Accumulation in the Serum as a Preliminary to Sweating, Am. J. Physiol. **74**: 205, 1925.
Adolph, E. F., and Fulton, W. B.: The Effects of Exposure to High Temperatures Upon the Circulation in Man, Am. J. Physiol. **67**: 573, 1924.
Bazett, H. C.: Physiological Responses to Heat: Changes Occurring in Mammals as a Result of Exposure to Environments of High Temperature—Especially in Man, Physiol. Rev. **7**: 531, 1927.
19. Hewlett, A. W.: The Effect of Room Temperature Upon the Blood Flow in the Arm, With a Few Observations on the Effect of Fever, Heart **2**: 230, 1910, 1911.
20. Barr, D. P., Cecil, R. L., and Du Bois, E. F.: Temperature Regulation After Intravenous Injection of Proteose and Typhoid Vaccine, Arch. Int. Med. **29**: 608, 1922.
21. Hewlett, A. W., and von Zwaluwenburg, J. G.: Rate of Blood Flow in the Arm, Heart **1**: 87, 1909, 1910.
22. Katz, L. N., Soskin, S., Schutz, W. J., Ackerman, W., and Plaut, J. L.: A "Metabolic Exercise Tolerance Test" for Patients With Cardiac Disease, Arch. Int. Med. **53**: 710, 1934.

Department of Clinical Reports

AN UNUSUAL T-WAVE IN AN ELECTROCARDIOGRAM

ROBERT H. HALSEY, M.D.
NEW YORK, N. Y.

IN THESE days, when much time is being devoted to the investigation and experimental study of the T-wave, it is important to have all recorded varieties on the record. With this in view the present communication is made. It was recorded nearly ten years ago; the whole episode occupied less than sixty seconds and, since it was observed, no other similar record has been seen, nor has there been found any mention of such an one in the literature of either clinical or experimental medicine.

The patient presented himself in May, 1926, complaining of brief attacks of tachycardia which had occurred at infrequent intervals. An attack on the preceding day had continued for an hour, and had made him so uncomfortable that it frightened him to such a degree that he was persuaded to seek advice.

He said he was forty-two years of age. He had had measles and chickenpox as a boy. He denied having had syphilis and said the Wassermann test had been negative. He had had gonorrhea and had received appropriate and effective treatment. He had had extractions of many of his teeth for pyorrhea and alveolar abscesses. He had had a chronically infected antrum which had been drained but not before he had developed a generalized arthritis, with some limiting of motion of most of his joints, including the maxilla. Because of frequent attacks of suppurative tonsillitis he had had a tonsillectomy at the age of thirty-six years. He admitted a liberal use of alcohol, tobacco, and coffee.

The examination showed a well-nourished man of good color, six feet four inches high, who weighed 210 pounds. He had considerable difficulty in moving because of the limited motion of his joints. He could separate his teeth about one centimeter. The breathing was normal, and there were no abnormal findings in the lungs. The peripheral arteries were not thickened, and the apex of the heart was felt in the fifth interspace, 10 cm. to the left of the midsternal line. The rhythm was regular at 68 per minute. The heart sounds were not abnormal, and there were no murmurs. The fluoroscopic cardiac shadow measured 13.6 cm., with the interthoracic wall measurement 28.3 cm. The aortic arch seemed somewhat denser than usual. The abdomen was not abnormal. The deep reflexes were present and active. The physical examination otherwise was negative.

The electrocardiogram (Fig. 1) taken on May 17 showed a regular sinus rhythm at a rate of sixty, a P-R conduction time of 0.16 sec., and a QRS duration of 0.08 sec. In Lead I, the P-wave was positive, 1 mm. in all cycles. The R-wave varied in voltage with respiration from 5 mm. to 9 mm., and the S-wave varied from 1 mm. to 2 mm. The T-wave was positive 1 mm. and recurred in the same form until the third cycle

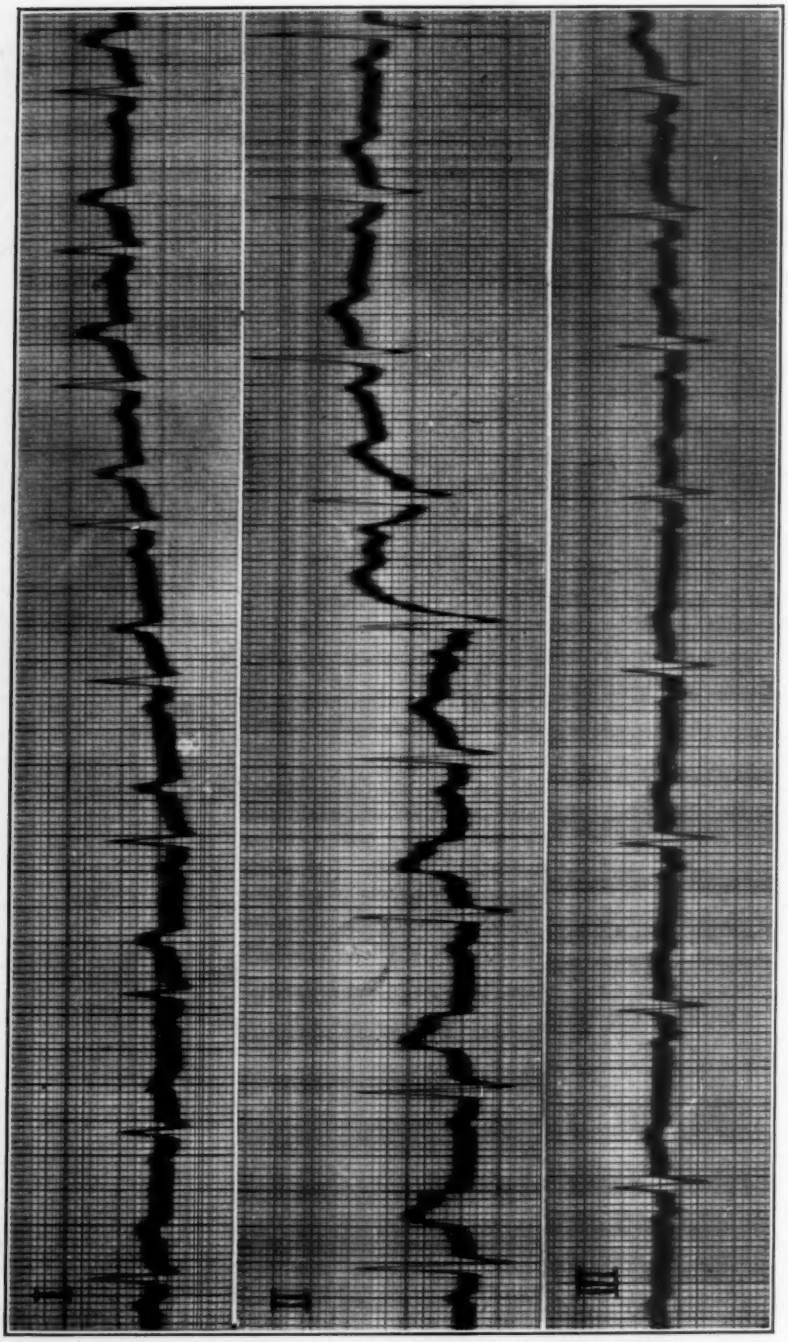

Fig. 1.—A. P. O. May 17, 1926.

in the figure, when there was an abrupt change consisting in an elevation to 3.5 mm. in height, and a sharpening in contour, gradually widening at the base and becoming blunter until, at a height of 5 mm., it had a peak at two levels and a base 0.12 sec. in duration. This truncated conelike form continued to the end of the record. Lead II shows a sequential sinus rhythm, with a P-wave of 1 mm. in height and 0.08 sec. in duration; an R-wave of 14 mm. to 15 mm., changing voltage with respiration; an S-wave of 5 mm. to 6 mm., the first limb being the downward continuation of the second limb of R. Following S is an isoelectric portion of about 0.12 sec. duration which at the end curves upward into a T-wave of two levels and a base of 0.22 sec. duration. This form of

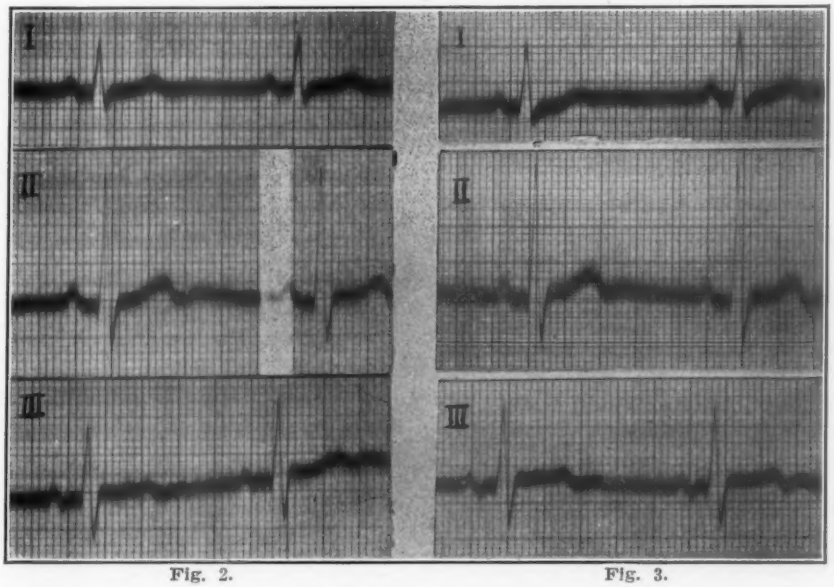

Fig. 2. Fig. 3.

Fig. 2.—A. P. O. May 21, 1926.
Fig. 3.—A. P. O. May 28, 1926.

T continues until there is an abrupt cessation and a return to a T-wave with a slow diphasic form, the first portion being positive for 3 mm. to 2.5 mm., and the second negative for 1 mm. The P-wave after the cessation of the abnormal T-wave has a different conformation. The elevation of the base line at this point may have been due to motion of patient's arm. Lead III reveals a sequential sinus rhythm, with a P-Q conduction time of 0.18 sec. P in the first cycle is diphasic but becomes completely positive with inspiration. R_3 varies from 7 mm. to 9 mm. The S-wave varies slightly with the changes in R. T is positive and diphasic, with a gentle curve.

While the first and second leads were being recorded, the patient said he had a "quivering feeling" in his left chest and put his hand up to the

precordium at about the moment of cessation. There was no objective change visible at the chest area or in vasomotor skin color changes.

Two subsequent records (Figs. 2 and 3) show no abnormal complexes though there is some increase in the voltage of the R-waves.

The patient has continued to carry on without further attacks or the development of any cardiac incapacity.

COMMENT

The unusual T-waves cannot be artefacts since they originate in Lead I and continue in relation to the T portion of the cycle through the Lead I time interval and during the short interval of changing leads into Lead II and up to its cessation in Lead II, with abrupt discontinuance. The phenomena were accompanied by subjective sensations.

The most plausible explanation from experience is the suggestion of a paroxysmal auricular tachycardia with two-to-one auriculoventricular block. There are several unusual features. The alternation in the time intervals from P to T and from T to P. The time P to T is regular and equal to 0.48 sec., but the T to P time varies from 0.4 sec. to 0.28 sec., as the diastolic time varies. The apex of T is a fixed time after P but there is a variable time interval between apex of T and the succeeding P. This indicates an unusual auricular-impulse-formation behavior if it originates in the sinus but is probably not unusual if it is inherent in the factors which cause T. When a P-wave falls on a T-wave, the summation of the two approximates that of the usual P degree but does not otherwise change the form of T. In the recorded T, the sum is much greater in voltage and much longer in duration and thus has the form of a truncated cone rather than a pyramid with smaller pyramid superimposed.

The conformation, time incidence, and duration suggest that the phenomena may be due solely to changes in that portion of the conduction system producing the T-wave and not to an algebraic summation of P plus T.

SUMMARY

The record presents a T complex differing in form from the expected complex of the algebraic sum of P plus T.

The conformation of the T resembles a summation occurring in a paroxysmal auricular tachycardia, with a two-to-one block. If this is true, the rhythm of the P-wave is not regular, though the time between the P and T is regular, for the time from T to P is variable.

The variations in the form of T and its increased duration suggest the conception of a disturbance in the function of that portion of the conduction system producing the T-wave.

After this report was prepared for publication, the opportunity presented and Dr. Harold E. B. Pardee examined the record and has kindly furnished the following note:

"The record shown me has one additional noteworthy feature which seems important. The QRS-T duration in Lead I varies between 0.40 and 0.42 sec. and does not change materially in most of the cycles showing the peculiar deformity of T. In the eighth cycle, however, it reaches 0.44 sec. In Lead II the QRS-T duration is 0.50 sec. in the cycles with deformed T and varies between 0.40 and 0.42 sec. in the others. In these prolonged cycles one can observe an appearance like the end of the T-wave at 0.42 sec. after the beginning of QRS. This suggests the presence of an artefact. If one could suppose that an extracardiac potential were developed at a point in the first beat of Lead II at 0.22 sec. after the peak of R and ended 0.44 sec. after this peak, having caused an elevation of about 4 mm. in the zero of the record for this length of time, one could explain this deformity. But such an extracardiac potential could not be developed so regularly with each beat in such an exact relation to the preceding QRS group. In Lead I its onset varies between 0.28 and 0.32 sec. after the beginning of QRS and in Lead II between 0.26 and 0.30 sec. after this event. It seems that for this reason we must attribute this peculiarity of T to some variation in the deactivation processes in the ventricular muscle."

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ELECTROCARDIOGRAPHIC CHANGES IN TRICHINOSIS*

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CASES of trichinosis with clinical and electrocardiographic evidence of myocardial damage are rare. Within the past year there have been two references in the literature to electrocardiographic changes in trichinosis.

There are in the literature a few references to involvement of the myocardium on histological examination in such cases. In one case a questionable trichina has been noted in the myocardium.[1]

Zoller[2] in an excellent article reports that it is impossible to find trichinae after the second week in the myocardium of guinea pigs. Dunlap and Weller[3] fed white rats trichinae larvae and noted that there was an absence of encysted larvae in the heart muscle. They believe that the active migration of the larvae to the myocardium, and not a toxic substance, produced the myocarditis. They are unable to explain the lack of encystment.

With these changes in the tissues it is surprising there are so few references in the literature to clinical changes. Spink[4] has recently given an excellent review of this subject. Master and Jaffe[5] have noted some electrocardiographic changes. Cheney[6] reports a case without signs of circulatory failure but with extreme hypotension. The electrocardiogram showed occasional extrasystoles.

A case of trichinosis has recently been observed in Lakeside Hospital with striking changes in the contour of the T-waves of the electrocardiogram. Pardee[7] mentions that T-wave changes may occur in trichinosis.

A well-developed, twenty-seven-year-old white man entered the accident ward at Lakeside Hospital in a stuporous condition. Twelve days before admission to the hospital, the patient was sick and vomited. He worked for three days and then had generalized aching and more frequent vomiting. The eyelids were swollen but the swelling subsided in two or three days. The day before admission he was somewhat stuporous and drowsy. His family physician stated that there had been some muscular twitching and some pain in the abdomen. Later history revealed the fact that the patient frequently ate cold pork pie and pigs' feet.

Physical examination revealed a stuporous man with loss of deviation of the eyes to the left. There was poor convergence. There was left hemiparesis, with hyperactive reflexes, a positive Babinski response, and ankle clonus. Left facial paralysis was present. The blood pressure was 88/68. The leucocyte count on admission was 26,500 with 62 per cent of eosinophiles. The blood and spinal fluid Wassermann reactions were negative. Spinal fluid revealed normal dynamics, negative Pandy reaction, and 3 lymphocytes per cubic millimeter. No trichinae were

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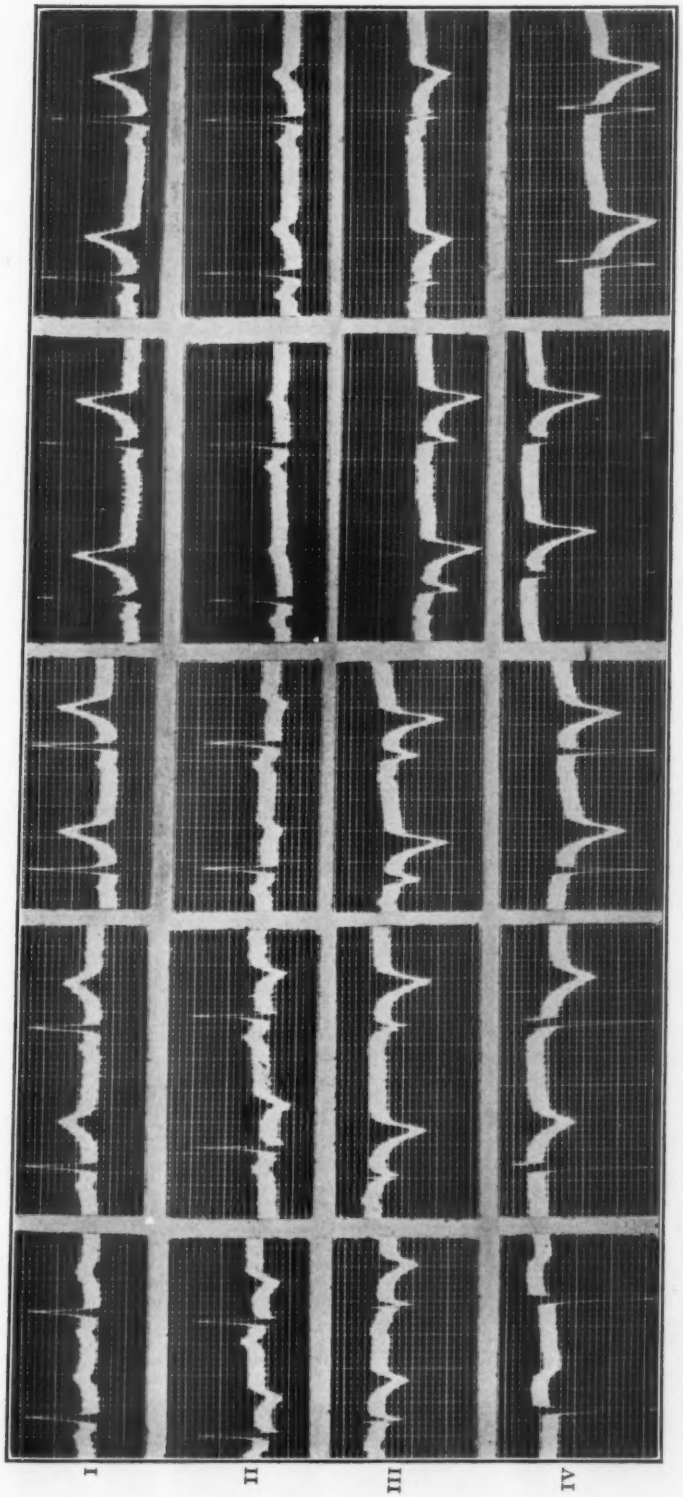
I
II
III
IV
July 9, 1934
a.
July 13
b.
July 23
c.
August 20
d.
December 4
e.

Fig. 1.

found in the spinal fluid. A biopsy of the deltoid muscle revealed an acute myositis and occasional encysted parasites. The patient's temperature was 39° C. on admission and fell to normal by the sixth day.

Throughout the first week of the hospital stay, the patient was stuporous and incontinent. He gradually improved and the abnormal neurological findings disappeared. He was discharged sixteen days after admission to the hospital with no abnormal neurological findings, and a blood pressure of 105/65.

A diagnosis was made of trichinosis of the somatic muscles, of the brain and the meninges and of the myocardium. The electrocardiograms showed variations in the T-waves. The first record, Fig. 1 (*a*) taken July 9, 1934, showed an inverted T-wave in the second and third leads of the "cove-plane" type. The fourth lead showed slight elevation of the S-T interval with an upright T-wave. Four days later (*b*) in the first lead the T-wave was higher; the T-wave in the third lead was more deeply inverted; and the fourth lead also showed an inverted T-wave. Ten days later (*c*) the first lead showed a higher T-wave, the second lead a shallow, inverted T-wave, the third lead no change, and the fourth lead a deeper T-wave. Six weeks subsequent to the first electrocardiogram (*d*) the second lead showed a slight elevation of the T-wave with no changes in the other leads. Five months after the first record (*e*) the T-wave in the second lead was slightly more elevated and in the third lead less deeply inverted. The last record, taken July 25, 1935, showed no change from that of December 4, 1934.

SUMMARY

A case of trichinosis with clinical and electrocardiographic evidence of myocardial involvement is reported. The T-waves in the electrocardiogram were inverted in the second lead and upright in the fourth lead. These changes gradually disappeared.

REFERENCES

1. Frothingham, C., Jr.: A Contribution to the Knowledge of the Lesions Caused by Trichina Spiralis in Man, J. M. Research **15**: 483, 1906.
2. Zoller, H.: Ueber die Herzmuskelentzundung im Verlauf der Trichinose, Virchows Arch. f. path. Anat. **265**: 430, 1927.
3. Dunlap, G. L., and Weller, C. V.: Pathogenesis of Trichinosis Myocarditis, Proc. Soc. Exper. Biol. & Med. **30**: 1261, 1933.
4. Spink, W. W.: Cardiovascular Complications of Trichinosis, Arch. Int. Med. **56**: 238, 1935.
5. Master, A. M., and Jaffe, H.: Electrocardiographic Evidence of Cardiac Involvement in Acute Disease, Proc. Soc. Exper. Biol. & Med. **31**: 931, 1934.
6. Cheney, G.: Sporadic Trichinosis With Extreme Hypotension, J. A. M. A. **86**: 1004, 1926.
7. Pardee, H. E. B.: Clinical Aspects of the Electrocardiogram, ed. 2, New York, 1928, Paul B. Hoeber, p. 82.

Department of Reviews and Abstracts

Selected Abstracts

Necheles, H., Frank, R., Kaye, W., and Rosenman, E.: Effect of Acetylcholine on the Blood Flow Through the Stomach and Legs of the Rat. Am. J. Physiol. 114: 695, 1936.

The stomach and hind legs of rats were perfused with Locke solution, to which various amounts of acetylcholine were added. In forty-five tests on the stomach, vasoconstriction was obtained forty-four times. The hind legs of rats showed vasodilation in five tests when perfused with acetylcholine. Atropine counteracted the vasoconstrictor effect of acetylcholine on the stomach in every case and the vasodilator effect on the hind legs in all tests but one.

E. A.

Wood, Paul: The Erythrocyte Sedimentation Rate in Diseases of the Heart, Quart. J. Med. 5: 1, 1936.

The erythrocyte sedimentation rate has been investigated in 164 cases of heart disease.

Congestive heart failure retards the sedimentation rate regardless of the cardiac pathology and may therefore mask activity of the disease process.

Increased sedimentation rates are found in cases of active rheumatic carditis, syphilitic aortitis, and myocardial infarction. The readings approach normal as the condition improves.

The sedimentation rate is also increased in cases of infective endocarditis and malignant hypertension, but the test is of little value in these conditions.

Angina pectoris of effort, apart from syphilitic cases, is associated with a normal sedimentation rate, angina of rest usually with a somewhat increased rate.

Normal sedimentation rates are found in cases of inactive rheumatic heart disease and of atherosclerosis.

In subjects with hypertensive heart disease the sedimentation rate may be normal or slightly increased.

Pulmonary infarction increases the sedimentation rate.

In the absence of cyanosis, cases of congenital heart disease are associated with a normal sedimentation rate, but with marked cyanosis the rate is abnormally slow.

Mild cases of thyrotoxicosis in which cardiac symptoms predominate are associated with normal sedimentation rates.

AUTHOR.

Behr, W.: The Onset and Duration of Diphtheritic Heart Involvement. Ztschr. f. Kreislaufforsch. 27: 793, 1935.

This is based on a study of 230 cases of malignant diphtheria studied clinically and electrocardiographically. Diphtheritic myocardial involvement usually occurs in the first two weeks of the disease. No evidence of new damage occurs after the twenty-first day. The prognosis is especially unfavorable when the heart damage occurs in the first week. The changes are degenerative in character with round cell infiltration. The mortality was 36.5 per cent in the entire series.

Recovery from damage to the heart is rapid, as a rule, when the child survives the infection. The only persistent damage seems to occur when the common bundle or its branches are involved.

L. N. K.

Winans, H. M., and Dunstan, E. M.: Heart Disease in North Texas. Texas State J. Med. **31:** 444, 1935.

The impression that rheumatic heart disease in this section of Texas is relatively low in incidence is confirmed.

The impression that, when found, preceding attacks of acute arthritis are relatively low is also confirmed. The percentage incidence of definite attacks of tonsillitis is probably no greater than might be associated with any other disease. Chorea is evidently a negligible part of the rheumatic picture as seen in this study.

Marks, Joseph H.: Calcification in the Annulus Fibrosus of the Mitral Valve. New England J. Med. **214:** 411, 1936.

The above report has been presented in order to record a proved case of calcification in the annulus fibrosus of the mitral valve which was correctly diagnosed by roentgen ray during life. It should be recalled that the annulus fibrosus is a figure-of-eight structure which surrounds both the mitral and tricuspid orifices, but the degenerative process which leads to calcification has been noted only in that portion which surrounds the mitral orifice; this is perhaps related to the greater amount of work done by the left side of the heart.

It should be noted that these areas of calcification can be demonstrated with any fluoroscope using 5 milliamperes of current at about 88 kilovolts provided that the examiner searches carefully the deeper parts of the heart through a small aperture and with his eyes fully accommodated. It is well to begin at the auriculoventricular groove on the left border and then gradually move inward and downward at an angle of about 45 degrees. If a mass of calcium is present, its characteristic dancing movement will be noted when the patient holds his breath. Once the mass is found, more accurate localization is made by gradually rotating the patient. Unless the heart rate is too rapid, the exercise of care and patience will be productive of good film records even though the more expensive high speed equipment is not available.

That intracardiac calcification may be diagnosed during life and that this calcification may be correctly localized is of real interest to the cardiologist. Difficulty is frequently encountered in establishing the diagnosis of aortic stenosis clinically, but a roentgen demonstration of calcification in the aortic cusps dismisses all doubt. Likewise a demonstrable mass of calcium in the annulus would aid in establishing the prognosis in cases of complete heart-block. The internist and cardiologist may thus expect more from the roentgenologist in the future than a mere statement as to the cardiac size and contour and the appearance of the lung fields.

Kommerell, Burkhard: X-ray Diagnosis of Calcified Heart Valves. Fortschr. a. d. Geb. d. Röntgenstrahlen **53:** 34, 1936.

The author describes the findings in ten cases of the calcified heart valves and the technic which should be used to reveal such calcification. The most important part of the examination is the screen examination since the routine film generally does not reveal these calcifications. It is important to use somewhat harder rays than are usually used for examination of the chest and to examine with a very small diaphragm. The observed field should not surpass the limits of the heart shadow. The author found the new hektophan screen which gives especially light

pictures very useful for this purpose. The requirements for the interpretation of this shadow as belonging to the valve are as follows:

1. It should be impossible to project the shadow of these calcifications outside the heart shadow.

2. The relation between the shadows of these calcifications and the heart border should not change during deep inspiration.

3. The movement of these shadows during the heart cycle should be greater than the movement of the heart border.

4. The extension of the movement of these shadows increases in the first oblique.

In order to fix the findings on the film the author recommends the technic used in duodenal examinations.

F. B.

Scott, R. W.: Systolic Murmur in Clinical Medicine and in Insurance Examination. Ohio State M. J. **31:** 943, 1935.

Excepting physiological systolic murmurs originating over the pulmonic area and extra cardiac respiratory murmurs, all apical and aortic systolic murmurs in adults merit consideration. The faint ones are usually but not invariably benign; louder ones are frequently associated with some type of cardiovascular disease.

An apical systolic murmur for years may afford the only clinical evidence of a damaged rheumatic mitral valve which may go on to stenosis or become the seat of the usually fatal subacute bacterial endocarditis. Aortic systolic murmurs are more often than not a sign of organic disease. The current clinical teaching that tends to disregard the significance of all systolic cardiac murmurs is just as unsound as the older view which associated every adventitious cardiac sound with organic disease. Somewhere between these two extremes lies the truth, and it is from this midposition that an evaluation of systolic murmurs should be attempted.

Kurtz, Chester M., Bennett, James H., Shapiro, Herman H.: Electrocardiographic Studies During Surgical Anesthesia, J. A. M. A. **106:** 434, 1936.

Electrocardiographic studies were made on 109 patients during 113 surgical operations under various anesthetic agents as follows: cyclopropane, 41; ether, 20; procaine, 13; ethylene, 11; nitrous oxide, 10; vinyl ether, 7; chloroform, 6; and tribrom-ethanol in amylene hydrate, 5. Electrocardiograms were taken as a routine before operation, at frequent intervals during the surgical procedure, during recovery, and ten hours after the operation.

Disturbances of rhythm constituted the most striking changes noted, sinus arrhythmia, extrasystoles, and downward displacement of the pacemaker predominating. A rapid and totally irregular ventricular action, apparently never recorded except under anesthesia, occurred in four cases. Complete heart-block was found twice and paroxysmal auricular fibrillation once. Arrhythmias appeared more frequently in abnormal than in normal hearts. The lowest incidence of arrhythmias occurred with procaine and the highest with chloroform. Of the entire series, only 21 per cent failed to show some type of disturbance. No constant and specific relationship could be established between the occurrence of arrhythmias and the depth of anesthesia or the steps in the surgical procedure.

Variations in the amplitude of the QRS complexes and T-waves, shifting of the ST segment and changes in the P-R interval occurred in the majority of cases and for the most part were of a transient nature.

In a large percentage of cases the electrocardiogram taken ten hours after operation differed in certain respects from the control tracings, and further work will be required to determine the persistence and significance of these changes.

AUTHOR.

Storti, E.: Concerning the Nullpotential-Electrode in Electrocardiography. Ztschr. f. Kreislaufforsch. 27: 830, 1935.

The possibility of using a nullpotential-electrode was investigated on an equilateral triangle model. The values of the potentials at the three corners of the triangle were determined, and by applying Kirschhoff's distribution equation, it was shown that the procedure of connecting the three ends of the triangle together as used in man by Wilson and his associates did not give a zero potential. The author demonstrates that the deviation from zero potential is a periodic function of Einthoven's angle alpha; zero potential being attained when the angle is 0 degrees, 60 degrees, and 120 degrees. The author concludes that the assumption that the electrode employed by Wilson, Johnson, MacLeod, and Barker is at zero potential requires proof in view of its inapplicability to the models used in his investigations.

L. N. K.

Luft, H.: Electrocardiographic Studies Concerning Left and Right Axis Deviation. Ztschr. f. Kreislaufforsch. 27: 793, 1935.

In twenty-nine out of one hundred instances of hypertension there was left axis deviation in the ordinary three leads. None of the twenty-one instances of emphysema showed right axis deviation. However, by utilizing precordial leads with the distant electrode on the right arm, a distinction could be made between these two types of cases. The procedure is to connect the right arm electrode to the right arm terminal and the precordial electrode to the left arm terminal. The maximum potential over the right and that over the left ventricle are determined and the ratio of the two is calculated. The ratio L/R in normals varies between 1.3 and 1.7. In forty-five out of fifty patients with hypertension this ratio was above 1.7. In all twenty-five patients with emphysema, mitral stenosis, or asthma the ratio was less than 1.3. This procedure, therefore, offers a better criterion of determining ventricular preponderance than that obtainable from the standard leads.

L. N. K.

Rabinowitz, H. M., and Kahn, J.: Relationship of Phospholipin Metabolism to Thromboangiitis Obliterans and Its Treatment. Am. J. Surg. 31: 329, 1936.

Based on the premise that the thrombotic tendency in thromboangiitis obliterans is due to changes in blood chemistry and coagulability, studies of the phospholipin metabolism have convinced the authors that the pathological process lies there. Although phospholipins are adequately mobilized in the blood stream, they are not properly stored or utilized in the formation of creatine phosphate used in muscle contraction. The changed lecithin-cephalin ratio predisposes to intravascular clotting. This metabolic defect explains the early claudication seen in this disease.

Since the authors have evidence that insulin-free pancreatic tissue extract contains a hormone which exerts a strong influence on phospholipin metabolism, they advocate in the treatment of thromboangiitis obliterans use of that extract plus limitation of lecithin-rich foods.

L. H. H.

Huber, H.: Acquired Defects of the Intraventricular Septum. Ztschr. f. Kreislaufforsch. 27: 825, 1935.

This is a report of two autopsied cases, both the result of a rupture following myomalacia due to coronary occlusion. Three other cases from the literature are cited. The acquired defects following myomalacia are located in the anterior apical or midportions of the septum. This is in contrast with congenital defects and acquired ones following endocarditis which are located toward the A-V junction.

L. N. K.

Ernstene, A. Carlton: The Differential Diagnosis of Coronary Artery Disease. J. Kansas M. Soc. **36**: 441, 1935.

In the past, in discussions of the differential diagnosis of angina pectoris and coronary thrombosis, emphasis has been placed almost entirely upon the fact that these conditions might give rise to symptoms suggestive of some other pathological state, particularly upper abdominal disease. Only of late have a few reports appeared directing attention to the possibility of erroneously interpreting the symptoms of upper abdominal disease and certain intrathoracic conditions as due to coronary artery disease.

In the present communication are summarized four cases in which the symptoms closely resembled those of coronary thrombosis or angina pectoris. In the first case the symptoms were due to cholelithiasis. In the second, a large esophageal hiatus hernia caused pain suggestive of angina pectoris. In the third, a clinical picture simulating coronary occlusions resulted from pulmonary embolism with acute cor pulmonale, and in the fourth, a dissecting aneurysm of the aorta was mistakenly diagnosed coronary thrombosis. The cases illustrate the diagnostic significance of negative electrocardiographic findings and also indicate the importance of detailed analysis of the patient's symptoms and physical signs. In the future diaphragmatic hernia, upper abdominal disease, dissecting aneurysm of the aorta, and pulmonary embolism with acute cor pulmonale should be excluded before a diagnosis of angina pectoris or coronary thrombosis is made in patients presenting features not typical of coronary artery disease.

Hochrein, Max: Guiding Principles in the Treatment of Myocardial Infarct. München. med. Wchnschr. **82**: 1515, 1935.

The diagnosis of myocardial infarct is relatively easy. The prognosis is very grave, the mortality being from 60 to 70 per cent in a large clinical series. Myocardial infarct is usually caused by coronary thrombosis. The author believes that coronary spasm resulting from vagotonia, especially if susceptibility to spasm is increased by nicotine, coffee, digestive disturbances, or meteorism, may be the cause occasionally. The immediate effects of infarction are increased irritability of the myocardium, early rise in blood pressure which is generally followed by a marked fall, evidences of circulatory shock, and certain chemical disturbances, such as occasional hyperglycemia and nitrogen retention in the blood.

The author advocates, in the early stages, sodium luminal 0.2 gm. intramuscularly two or three times a day followed by some other sedative orally on succeeding days. He prefers sodium luminal to morphine as he claims the former improves cardiac circulation. Bed rest is recommended for at least six weeks. Small meals at two-hour intervals are suggested. Intramuscular injection of sympatol 1.0 c.c. is advocated as a circulatory tonic in the early stage, and 20 drops by mouth three times a day is suggested for later use. An attempt to avoid fibrillation by the use of quinidine 0.1 gm. twice a day is suggested. Cardiac failure should be treated by digitalis or intravenous injection of strophanthus and of glucose.

W. B.

Rinehart, James F.: Studies Relating Vitamin C Deficiency to Rheumatic Fever and Rheumatoid Arthritis; Experimental, Clinical, and General Considerations. Ann. Int. Med. **9**: 671, 1935.

The experimental basis for the concept that rheumatic fever may be the result of the combined action of vitamin C deficiency and infection is reviewed. Further experimental studies are reported which confirm the original observations that this deficiency with superimposed infection produces in the guinea pig a disease state with many pathological similarities to rheumatic fever. Comparable lesions develop

in the heart valves, the heart muscle, and the joints. The occasional occurrence of subcutaneous nodules remarkably like those of rheumatic fever would appear to complete the pathological similarity.

Evidence is presented that the factor of infection is not specific. Essentially similar lesions develop when different organisms are used as the infecting agents. The same infections do not cause rheumatic type lesions in animals receiving adequate amounts of vitamin C.

It is suggested that vitamin C deficiency may afford the basis for the hemorrhagic manifestations frequently observed in rheumatic fever.

The epidemiological peculiarities of rheumatic fever, notably its social, geographic, and seasonal incidence, might be explained on the operation of a scorbutic factor in the disease.

Evidence indicating not only the existence, but the probable frequent occurrence of latent scurvy is reviewed. The relatively high vitamin C requirements of children, the limited capacity to store the vitamin, and the possible influence of infection or fatigue in depleting this organic reserve are discussed.

Clinical studies in progress are cited that have afforded encouraging data.

On the basis of further experimental studies and clinical and epidemiological data, the thesis is reaffirmed that rheumatic fever may result from the combined influence of vitamin C deficiency and infection.

Gerlach, W.: Rheumatic Mesaortitis. Ztschr. f. Kreislaufforsch. 28: 2, 1936.

The author discusses the differentiation between syphilitic and rheumatic mesaortitis and reports an autopsied case which is interpreted as being rheumatic mesaortitis with dilatation of the ascending aorta and aortic arch.

L. N. K.

Beck, E. C., Fowler, J. G., Koenig, E. C., and Bowen, B. D.: Vascular Disease in the Obese Diabetic, and in Non-Diabetics; A Discussion of Arteriosclerosis as a Cause of Diabetes. Ann. Int. Med. 9: 662, 1935.

Calcification of the arteries of the lower extremities (demonstrated roentgenologically), which is common, particularly in patients with older, uncontrolled cases of diabetes, is essentially absent in patients with early cases of diabetes and in obese people, some of whom are potential diabetics.

No evidence was found to show that hypertension or retinal arteriosclerosis could be correlated with the obese patient's ability to use glucose. The incidence of hypertension appears to be higher in the older diabetic. We believe, however, that this is essentially related to obesity and not to diabetes.

The proposal that diabetes in older people is commonly caused by sclerosis of the pancreatic blood vessels is discussed. Direct proof that sclerosis of the pancreatic vessels causes diabetes cannot be determined by clinical methods, nor can it be held responsible as a primary cause of diabetes when found at necropsy. Nevertheless, it seems improbable that such sclerosis can be regarded as a general cause for diabetes in older people.

Elliot, A. H., and Nuzum, F. R.: Cholesterol Content of Whole Blood in Patients With Arterial Hypertension. Arch. Int. Med. 57: 63, 1936.

The significant finding in this carefully controlled piece of clinical investigation is that uncomplicated arterial hypertension is not accompanied by significant changes in the cholesterol content of the blood.

The cholesterol figures of 53 hospitalized hypertensive patients followed very closely those of a control group of 45 hospital and dispensary patients.

Vascular degeneration and renal impairment associated with the hypertension do not raise the cholesterol level of the blood.

L. H. H.

Gregg, Donald E.: The Phasic and Minute Coronary Flow During Acute Experimental Hypertension. Am. J. Physiol. **114**: 609, 1936.

Acute experimental hypertension produced by increasing the peripheral resistance, either mechanically or chemically, augments the coronary blood flow. It is the author's tentative concept that as the aorta is compressed and the blood pressure and pulse pressure rise, the heart rate slows, the coronary systolic resistance decreases relative to the aortic systolic, thus permitting an actually greater inflow per beat during ventricular contraction, although the systolic flow relative to the diastolic is decreased. However, the minute systolic flow increases only moderately since, as the heart rate slows, the time occupied by systole is materially reduced. During diastole at the high pressure the diastolic interval lengthens, and the diastolic coronary pressure increases only slightly, with the net result that the diastolic flow per cycle and per minute is tremendously augmented. The conclusion is reached that the dominant factor in increasing the myocardial blood supply in acute experimental hypertension is a combination of mechanical changes, of which the most important is the aortic head of pressure throughout the cycle, together with the relative increase in the time per minute occupied by diastole.

E. A.

Gammon, George D.: The Carotid Sinus Reflex in Patients With Hypertension. J. Clin. Investigation **15**: 153, 1936.

In a study of thirty-one patients with hypertension of either the essential type or that associated with arteriosclerosis, the carotid sinus nerve endings were found, in accordance with other observers, to cause a depressor reflex when stimulated directly. The response to changes in intravascular pressure within the sinus, contrary to the findings of others, was in the direction usually obtained in normal persons. These observations indicate that a failure of the carotid sinus mechanism is not the cause of hypertension in these patients. The significance of these findings is discussed in relation to nervous factors concerned in hypertension.

Clute, H. M.: Acute Arterial Obstruction From Arteritis. New England J. Med. **214**: 137, 1936.

The condition described in two cases and cured operatively by the author is one of complete occlusion of a large arterial trunk by an inflammatory process within the vessel. Acute arteritis, being localized, is not to be confused with thromboangiitis obliterans or the chronic occlusive diseases.

The increase of blood supply to the part following resection of the affected area of the vessel is thought to be due to paralysis of the vasomotor nerves to accessory arteries, according to the contention of Leriche. Clute believes that the vasospastic sympathetic nerves are stimulated by the diseased artery.

L. H. H.

Jones, Tudor: The Structure and Mode of Innervation of Capillary Blood Vessels. Am. J. Anat. **56**: 227, 1936.

There is nothing exceptional in the histological constitution of the capillary blood vessels. They consist essentially in a neuromuscular mechanism of the same nature as the walls of the larger vessels and contractile viscera generally. Rouget's cells belong to the nervous, not to the contractile, element in this complex. The contractile elements are ordinarily smooth muscle cells. The first sign of physiological activity in young vessels is the extension of elements in continuity with the nervous system in their neighborhood.

E. A.

Russow, E.: The Blood Supply of Hypertrophic and Atrophic Hearts. Zeitschr. f. Kreislaufforsch. **28**: 41, 1936.

The total cross-section area of the three main branches of the coronary is increased in hypertrophied hearts and decreased in atrophied ones, and there is a parallelism between heart weight and the total cross-section area so measured. The media of the coronary arteries, but not the intima, is increased in thickness when the arterial pressure is elevated. Apparently, when advanced coronary arteriosclerosis is absent, the blood supply of hypertrophied heart is better than that of the normal as far as the caliber of the large coronary arteries is concerned. This report is based on a study of 45 hearts.

L. N. K.

Kommerell, Burkhard: Symptomatology of Aneurysms of the Abdominal Aorta. Röntgenpraxis **8**: 25, 1936.

This is a report of one case in which the x-ray examination showed a tumor mass which pushed forward the cardial part of the stomach and produced a narrowing of the cardia. The necropsy revealed a dissecting aneurysm of the abdominal aorta.

F. B.

Putts, B. Swayne, and Bacon, Ralph D.: Large Aneurysm of the Descending Thoracic Aorta With Retropsoas Extension. Am. J. Roentgenol. **35**: 59, 1936.

A case is reported of aneurysm of the lower thoracic aorta in a woman. The aneurysm had been demonstrated roentgenologically for more than four years and probably had been present for at least eight years. It originated from the posterior wall just above the diaphragm and extended behind the diaphragm at its last vertebral attachment to become largely a retropsoas mass. The aneurysm caused erosion of the lower four dorsal and the first lumbar vertebrae and the eleventh and twelfth ribs.

E. A.

Bell, James: Blood Pressure and Aortic Aneurysms. Irish J. M. Sc. Dec., 685, 1935.

The factors responsible for the difference in the systolic blood pressure of the brachial arteries associated with aortic aneurysm are: (1) occlusion of the orifice of the innominate or left subclavian artery, due to the distorting effect of the aneurysm or to blood clot, (2) diminution in amplitude of the pulse wave, produced by passage through the aneurysm, and (3) loss of kinetic energy in the aneurysm.

E. A.

Strombeck, J. P.: The Late Results of Embolectomy Performed on Arteries of the Greater Circulation. Acta chir. Scandinav, **77**: 229, 1935.

In a series of 327 operations performed in Sweden from 1912 to 1932 for the removal of emboli from the arteries of the greater circulation, 63 per cent of the patients died in hospital, 18 per cent were discharged improved after amputation, and 19 per cent had good circulation on discharge. Three-fourths of the latter successful cases were alive one year after the operation, one-half after three years, one-third after five years, and one-eighth after ten years. The length of the survival period seems to depend particularly upon the character of the cardiac affection and also upon the age of the patients, as well as the more accidental factor of danger for new emboli. There is a striking tendency toward cerebral circulatory disturbances (probably emboli in most cases) and emboli in the viscera and extremities long after the first embolism.

Working capacity was best in those who had sufficient vitality to survive the procedure for a fairly long period. Among the half of the series who lived more than three years after a successful operation, about 30 per cent enjoyed rather good working capacity while 20 per cent could not work at all. About 10 per cent of the other half of the patients with successful cases who died in less than three years after operation were able to work rather well for some time, but at least 70 per cent were quite incapable of working.

The local result in the portion of the body operated upon was in most cases very good. Small areas of necrosis, sensory disturbances, or peroneal pareses occurred in one-eighth of the cases, and mild subjective symptoms, such as numbness and paresthesia, in about one-half.

Gurin, David, Bulmer, J. W., Derby, Richard: Dissecting Aneurysm of the Aorta. New York State J. Med. **35**: 1200, 1935.

A case is reported in which surgery relieved arterial obstruction of an extremity due to a dissecting aneurysm of the aorta. A diagnosis of the occlusion of the right external iliac and femoral arteries had been made. It was felt that, in spite of marked hypertension and cardiovascular and renal damage, the operation might prevent an otherwise inevitable gangrene of the extremity.

Two and a half hours after the onset of symptoms the right femoral artery was exposed under local anesthesia. At the beginning of the operation a faint pulsation could be felt in the femoral artery. On exposing the vessel no pulsation was visible or palpable. Its wall was intact, and no mass could be felt in the lumen. Aspiration with a fine needle revealed bright blood under markedly diminished pressure. The wound was closed, and under nitrous-oxide oxygen and ether anesthesia the abdomen was opened. The right external iliac artery when isoalted three inches above Poupart's ligament was found to have an infiltration of dark blood in its lateral third, extending as far as could be seen in both directions. An impact was transmitted along the artery from above with each heartbeat, but there was no expansile pulsation in any part of the vessel. Rubber-padded clamps were placed on the artery above and below to prevent any influx of blood. Then a longitudinal one-inch incision was made into the anterior surface, which appeared unaffected by the hemorrhagic extravasation. Upon opening the vessel, an atheromatous mass was encountered completely plugging the lumen, which had been narrowed by the dissecting hemorrhage. The intima and media opposite the atheroma were incised from within the vessel. A small curved Kelly clamp was inserted through this incision into a space between the media and adventitia. From this came a steady flow of dark unclotted blood. With the escape of this blood the obstruction was relieved, and when the proximal clamp was momentarily released, there occurred a spurt of bright arterial blood from the incision. The incision into the vessel was closed with interrupted suture of greased silk. When the clamps were removed an expansile pulsation was visible throughout the external iliac artery.

The diagnosis of dissecting aneurysm should be suspected when an individual, usually male, usually with history or evidence of severe hypertension, suddenly develops pain at the level of the precordium without evidence of acute myocardial damage by the electrocardiogram, fall in blood pressure, or marked rise in pulse. Often the pain in these cases is more severe over the thoracic spine or in the epigastrium than under the sternum. The diagnosis should be made when, following the above, signs of acute arterial blockage or internal hemorrhage develop.

Kinsman, J. Murray, and Moore, John Walker: The Hemodynamics of the Circulation in Hypertension. Ann. Int. Med. **9**: 649, 1935.

Using the dye-injection method of measuring the cardiac output and related factors, the authors studied 44 cases with normal cardiovascular systems, and 75 cases of hypertension subdivided into: 14 "undecompensated" cases which had never shown any signs or symptoms of congestive failure; 18 slightly, 7 moderately, and 15 severely "decompensated" cases; and 21 "compensated" cases, which had previously been decompensated, but which at the time of the test were perfectly compensated.

A large number of the functions of the circulation were studied simultaneously.

In hypertension in which congestive failure has never appeared the venous pressure is nevertheless likely to be definitely increased over normal, and the vital capacity reduced; the velocity of blood flow, the cardiac output, the stroke volume, and the number of heartbeats required to clear the heart and lungs of blood are essentially unchanged, while the work of the heart is tremendously increased.

As congestive failure appears and increases, the venous pressure progressively rises and the vital capacity falls; the velocity of blood flow becomes very markedly reduced; the cardiac output and stroke volume are greatly diminished; the number of heartbeats required to clear the heart and lungs of blood is markedly increased; and the heart work becomes reduced even to far below the normal value.

As compensation becomes reestablished, there is a tendency for all these functions to return toward normal, and the venous pressure does return to normal, but the vital capacity remains considerably reduced, as do the velocity of blood flow, the cardiac output, and the stroke volume; the number of heartbeats required to clear the heart and lungs of blood remains considerably increased, but the heart work becomes normal again or nearly so.

The results for volume of actively circulating blood in heart, lungs, and great vessels and total circulating blood volume are not striking but are parallel. In general, before congestive failure develops, there is no essential change in either; as congestion develops, they both progressively increase slightly; as compensation becomes reestablished, they increase greatly and significantly.

These results apply to the group as a whole. Individual cases show marked variations from the trend of the group as far as isolated functions are concerned, as, for example, a large output with a low vital capacity and a high venous pressure. This calls attention to the necessity of studying many of the functions of the circulation simultaneously, instead of only a few.

In the decompensated cases, rest alone causes a definite improvement in most of the functions enumerated, but the improvement from digitalis is very much more marked.

AUTHOR.

Wohl, Michael G., and Ettelson, L. N.: III. Studies in Obesity: Effect of Dinitrophenol on Blood Velocity. J. Pharmacol. & Exper. Therap. **55**: 439, 1935.

In 33 obese patients, the arm-to-tongue circulation time was measured by the intravenous saccharin method. The average of the group was 13.3 seconds, essentially normal figures.

In fourteen of the group dinitrophenol (1-2-4) was given, and further determinations of the circulation time were made. In seven patients an increase in blood velocity was noted, the average acceleration being 3.3 seconds per patient.

Further studies are indicated to determine the manner in which such speeding up of the blood flow is brought about.

Gauer, O.: Pulse Wave Velocity in the Aorta and the Arteries of the Leg of Man. Ztschr. f. Kreislaufforsch. **28**: 7, 1936.

Optically recorded pulses from the subcalvian artery along the course of the abdominal aorta and the femoral arteries were made. The time of the rise of the pulse wave in these various locations was determined. As a result of 250 measurements on a twenty-four-year-old healthy male subject, the author concludes that the pulse wave velocity is the same in the thoracic aorta when standing and reclining, viz., 3.8 to 4 meters per second. In the leg arteries the pulse wave velocity is 12 to 13 meters per second when the subject is standing and below 8.5 meters per second when the subject is reclining. The observations were confirmed with only minor variations in a second normal subject. The pulse wave velocity in the peripheral vessels is modified greatly and abruptly by light pressure.

L. N. K.

Markovits, F.: Estimation of Blood Volume by Means of Blood Sugar Determinations. Ztschr. f. Kreislaufforsch. **28**: 17, 1936.

Blood sugar is determined by the Hagedorn-Jensen's method on an empty stomach. Then 10 c.c. of 40 per cent dextrose solution is injected intravenously, and the blood sugar is determined 2 minutes later. The blood volume is calculated by dividing 40,000 by the milligram percentage rise in the blood sugar. This method was found to check fairly well in one rabbit with the blood volume value determined by bleeding, and in ten human subjects gave values equal to 1/12 the body weight.

L. N. K.

Tetelbaum, A. G., Umanski, S. I., and Krynski, M. I.: The Influence of Physical Exertion on Venous Pressure in Health and in Cardiac Failure. Wien. Arch. f. inn. Med. **28**: 121, 1935.

The authors used a direct venous pressure method. The needle was inserted in a cubital vein with the patient in the supine position. The exercise consisted in raising both legs 45 degrees above horizontal and maintaining this position for one minute with the knees straight. Venous pressure was estimated at frequent intervals after the legs were lowered. Eighteen subjects were studied: six normal persons, and six with moderate congestive heart failure, and six with severe congestive heart failure.

A rise of pressure of 30 to 50 mm. of saline with a rapid return to normal was observed after the exercise test in the six normal subjects. A higher rise (90 to 150 mm. and 105 to 160 mm.), was found respectively in the patients with moderate and those with severe heart failure. If the condition of the patient improved, the venous pressure rise approached the normal. If the condition of the patient became worse, the venous pressure changes became more abnormal. It was found that the venous pressure returned to the control level in 10 to 15 seconds after the exercise in normal persons and in from 35 to 70 seconds or longer in instances of cardiac failure. The duration of the venous pressure rise became shorter when the patient improved and became more prolonged when the patient's condition became worse. The authors consider this test of value in the study of cardiac failure.

W. B.

Henderson, Yandell, Oughterson, A. W., Greenburg, L. A., and Searle, C. P.: Muscle Tonus, Intramuscular Pressure and the Venopressor Mechanism. Am. J. Physiol. **114**: 26, 1936.

A technic for determining pressure within a muscle is described and is used to show variations in tonus. This tonic intramuscular pressure was found to be a prime factor in the venous return of blood to the heart. By means of Riml's experiment, particularly on a sympathectomized animal, it is shown that tonic elasticity of tissues is sufficient to squeeze a considerable part of the blood in the body out through the veins under a pressure corresponding to a column of blood of 10 to 12 cm. The tonic tissue pressure throughout the body combined with the negative pressure in the thorax, which is largely dependent upon the tonus of the respiratory muscles, determines the "effective venous pressure" that in health assures the venous return. Failure of the circulation in illness and after physical injuries and surgical operations is largely due to diminution of general body tonus and stagnation of blood in the flaccid tissues.

E. A.

Wilson, Harwell, and Roome, Norman W.: The Effects of Constriction and Release of an Extremity; An Experimental Study of the Tourniquet. Arch. Surg. **32**: 334, 1936.

Experiments were performed on nineteen dogs in an effort to study the effects of prolonged constriction of a limb. One hind limb was ligated by means of a rubber tourniquet for a period of from two to twenty hours under barbital anesthesia and then released. Of these animals 69 per cent died in an average interval of twenty-five and three-fifths hours after release of the constrictor, while only 17 per cent of a control series died. No animal with a leg constricted for less than three hours died, while several animals with a leg constricted for a period in excess of six and one-half hours died.

It was thought that the reactive hyperemia of the constricted limb and the absorption of metabolites from the limb were probably responsible for the primary transient depression of the blood pressure when the constrictor was removed, but that the secondary and more serious fall of blood pressure was occasioned by swelling of the damaged extremity by transudation and the consequent diminution of the circulating blood volume. The absorption of the products of anaerobic bacteriolysis of the tissues is another possible factor in the lowering of the blood pressure, but no positive proof or denial of its importance can be adduced from the present experiment. Survival of the animal after prolonged constriction of a limb was obtained by amputation of the limb followed by transfusion of blood but not by transfusion or by amputation alone.

E. A.

Allen, E. V., and Brown, G. E.: Intermittent Pressure and Suction in the Treatment of Chronic Occlusive Arterial Disease. J. A. M. A. **105**: 2029, 1935.

The authors present an evaluation of alternating negative and positive pressure in the treatment of obliterative arterial disease based on an analysis of cases in the literature and on their experience with 60 patients treated routinely with the pavaex apparatus developed by Herrmann and Reid. Thirty-two of the patients received sufficiently long periods of therapy to allow a preliminary estimate of the value of the method as used in the Mayo Clinic.

Allen and Brown are unable as yet to answer the question, "Do good results follow passive vascular exercise more frequently than other methods of treatment?" Their opinion is that "good results ordinarily follow changing environmental pressure treatment in cases in which good results could be expected from other measures and that when good results do not follow other measures, passive vascular exercise is usually valueless."

The pavaex method, however, "has been some contribution to the program of treatment." The greatest benefit observed by Allen and Brown is in the relief of the pain of ischemic neuritis.

L. H. H.

Symposium on the Autonomic Nervous System

Kuntz, A.: The Autonomic Nervous System: Essential Anatomy. J. A. M. A. **106:** 345, 1936.

This presentation begins a symposium on the autonomic nervous system at the 1935 meeting of the American Medical Association. Its chief value lies in orienting one as to the basis for the various operations on the sympathetic nerves and ganglia.

Davis, L., and Pollock, L. J.: The Rôle of the Autonomic Nervous System in the Production of Pain. J. A. M. A. **106:** 350, 1936.

Continuing the symposium, the authors discuss the chief theories of the relation of the autonomic system to pain. They conclude that the only proved contribution of the autonomic system to pain is in the utilization of the efferent fibers in certain of the referred types.

Brown, G. E.: Clinical Tests of Function of the Autonomic Nervous System. J. A. M. A. **106:** 353, 1936.

As knowledge of the rôle played by the sympathetic and parasympathetic nervous systems increases, and therapeutic measures become more efficient, tests for the functional imbalance of these systems become essential. Brown has gathered together the important types of test so far evolved through which objective comparison of abnormal to normal function can be made.

Jackson, D. E.: Essential Pharmacology of the Autonomic Nervous System. J. A. M. A. **106:** 357, 1936.

A brief consideration of the various drugs whose action on the autonomic system has been demonstrated.

Adson, A. W.: Indications for Operations on the Sympathetic Nervous System. J. A. M. A. **106:** 360, 1936.

Adson closes the symposium on the autonomic nervous system by discussing the rationale of sympathetic surgery in such conditions as Raynaud's disease, scleroderma, rheumatoid arthritis, hyperhidrosis, essential hypertension, and certain types of pain. The presentation is an excellent summary of what may be expected in this new field in the hands of expert surgeons.

L. H. H.

Dotti, Enrico: Experimental Studies of the Function of Lymphatic Vessels and Lymph Glands With X-ray After Subcutaneous Injection of Thorium Dioxide. Fortschr. a. d. Geb. d. Röntgenstrahlen. **50:** 615, 1934.

Roentgenological studies of lymph glands and lymphatic vessels of the legs of guinea pigs show that in diseases due to secondary infection of the lymph glands and vessels a less pronounced x-ray shadow is obtained after subcutaneous injection of thorium dioxide. It seems that the infection reacts on the reticuloendothelial system, reducing its ability to retain the electronegative thorium dioxide and decreasing the permeability of the lymph vessels.

J. K.

Ernst, Curt: Localized Edemas in Human Beings. Deutsche med. Wchnschr. 61: 745, 1935.

Vasoneurotic and hypertonic (red hypertonic) patients are predisposed to developing local edemas in the skin and mucous membranes. Capillary examination of several hundred vasoneurotic and hypertonic patients showed characteristics of spastic-atonic capillaries. But the local edemas are not due only to the changes of the minute vessels; there are also present typical changes in the skin tissue. The elasticity of the skin is decreased; measured with an elastometer (Schade), it showed a decrease in elasticity from 14 per cent to 38 per cent. Intracutaneous injection of 1:1,000,000 solution of morphine gave in this type of patients a more pronounced reaction, more lasting and larger wheals and redness, suggesting an increased amount of fluid in the skin. Intracutaneous histamine injection showed increased capillary permeability.

Vasoneurotic individuals are predisposed to certain diseases such as gastric ulcer, red hypertension, Raynaud's disease, ulcerative colitis, Ménière's disease, and certain types of asthma, cystitis, and glaucoma.

J. K.

Behnke, Albert R., Shaw, Louis A., Messer, Anne C., Thomson, Robert M., and Motley, E. Preble: The Circulatory and Respiratory Disturbances of Acute Compressed Air Illness and the Administration of Oxygen as a Therapeutic Measure. Am. J. Physiol. 114: 526, 1936.

Nitrogen emboli were produced in the blood of anesthetized dogs by rapid decompression from air compressed to 65 pound gauge pressure for 105 minutes. Rapid breathing, temporary rise followed by a fall in the blood pressure, retarded pulse rate, oxygen unsaturation of the arterial blood, and a marked increase in the arteriovenous difference were noted. The rapid breathing and unsaturation of the arterial blood are attributed to embolic blockage of the pulmonary circulation, and the fall in blood pressure and increased arteriovenous difference are attributed to embolic injury to the nerve tissue which controls circulation.

E. A.

Smith, Fred M., Rathe, H. W., and Paul, W. D.: Theophylline in the Treatment of Disease of the Coronary Arteries. Arch. Int. Med. 56: 1250, 1936.

It is important that measures be directed toward the restoration and maintenance of an efficient coronary circulation in the treatment of disease of the coronary arteries. The preparations of theophylline have a marked dilating action on the coronary vessels in the experimental animal, and clinical experience has demonstrated that they are valuable therapeutic agents in the treatment of disease of the coronary arteries, regardless of whether the cardiac disability is expressed by congestive failure, paroxysmal dyspnea, angina on effort, or occlusion of the coronary arteries. Questionable results and failures are encountered, but this is to be expected in the more advanced forms of the disease. Theophylline should be prescribed as soon as the diagnosis of disease of the coronary arteries is established, and its administration should be continued for a long period, in order to insure the maximum benefit from the medication. It should be remembered, however, that this constitutes only one measure in the treatment and, except for experimental purposes, should not be employed to the exclusion of other established means of restoring the cardiac function.

AUTHOR.

Book Reviews

THE DIAGNOSIS AND TREATMENT OF DISEASES OF THE PERIPHERAL ARTERIES. By Saul S. Samuels, A.M., M.D., New York, 1936, Oxford University Press.

This work is of undoubted value because it represents a strong brief for the conservative treatment of peripheral arterial diseases. In it the author has set forth evidence in the form of case reports, both singly and grouped, of patients suffering from thromboangiitis obliterans and arteriosclerosis obliterans, treated by conservative methods with excellent results.

The title of this volume, however, is somewhat misleading. Instead of a well-balanced presentation of the diseases of the peripheral arteries, in which space is allotted to each group according to its relative importance, we find the following distribution: In a volume of 254 pages, 148 pages are devoted to thromboangiitis obliterans, 48 pages to arteriosclerosis obliterans, 5 pages to Raynaud's disease, and 2 pages each to erythromelalgia and essential thrombophilia. Syphilitic arteritis, embolism, acrocyanosis, scleroderma, and polycythemia with vascular complications are merely mentioned, and there is no reference to lead sclerosis or rheumatic arteritis. Most of the diseases are mentioned for the purpose of differential diagnosis only. The book is really a monograph on thromboangiitis obliterans, with a discussion of arteriosclerosis obliterans included.

The description of thromboangiitis obliterans, a disease with which the author has had considerable experience, is very good. When it comes to treatment, however, the author merely presents his form of therapy, and condemns either by direct statement or by faint praise other recognized forms. All workers in this field will agree with his demand for complete abstinence from smoking, but the attitude that saline, given intravenously, is the one acceptable form of therapy to stimulate the circulation will be questioned by those who use citrate and by the large number of workers who have found typhoid vaccine, intravenously administered, to be the most satisfactory form of therapy for this purpose. His approach, moreover, shows a lack of understanding of the correct use of typhoid vaccine. The reviewer could find no mention of hepatitis or other complications which sometimes occur with saline therapy.

Although Raynaud's disease may have been relatively rare in Dr. Samuel's clinic, other vascular clinics are finding it very frequently, in varying degrees of severity. A more detailed consideration should therefore be given to it in a volume presuming to cover the entire field of peripheral arterial diseases, even though it is recognized that the defective mechanism may be in the nervous supply to the arterial system.

If this volume, in spite of its defects, will encourage physicians to have patience and courage enough to be conservative in the treatment of arterial disease, many extremities and, indeed, lives will be saved each year.

I. S. W.

LA TENSION MEDIANA DINAMICA: ESTUDIO CRITICO (CLINICO Y EXPERIMENTAL). By Dr. Angel Cammaroto. Buenos Aires, 1935, El Ateneo, 169 pp.

Dr. Cammaroto in this work, the thesis for his doctorate, presents the results of a detailed study of median dynamic tension, a subject which is of rather limited interest. The volume is generously illustrated and well printed on good paper.

After chapters on historical aspects of the subject, definition and method of determining the median arterial tension, the normal tension and its variations, he considers the median dynamic tension in relation to aortic insufficiency, arterial hypertension, hypotension, bradycardia, aneurysms, and hyperthyroidism. He then discusses solitary median hypertension, reviews the subject critically, and presents his conclusions which are as follows: The median tension varies within wide limits as do the systolic and diastolic pressures. Within the space of a few minutes it can vary rapidly. It appears to be related, at least in part, to vasomotor innervation. It is usually related to the extremes of blood pressure even when its relation to the diastolic pressure is more evident. It does not appear to be of particular interest in prognosis or in diagnosis. Median hypertension was not found as an isolated sphygmomanometric observation. The results obtained with the compensating manometer lack exactitude, and hence experimental contributions must be regarded as of doubtful value.

E. H.

ÉTUDE ANATOMO-RADIOLOGIQUE DE L'APPAREIL CIRCULATOIRE PAR OPACIFICATION POST-MORTEM: INTÉRÊT, TECHNIQUE, ET VALEUR DE CETTE MÉTHODE. By Pierre Hebert. Paris, 1935, Librairie E. Le François, 75 pp. with 13 figures.

ANATOMIE RADIOLOGIQUE DES CAVITÉS CARDIAQUES ET DU PÉDICULE VASCULAIRE. By R. Heim de Balzac. (Reprinted from Leçons de Cardiologie Faites à l' Hôpital Broussais.) Paris, 1935, Gaston Doin & Cie., 24 pp. and 23 figures.

These two brief studies are based on a large amount of painstaking work undertaken in order to establish more accurate knowledge of the x-ray appearance of the heart and the great vessels. The studies were made on the cadaver by means of the injection of an opaque material into the right and left sides of the heart separately, followed by careful radiological study. This method allows the visualization of the two sides of the heart separately but is not intended for or suitable for clinical use.

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